maXis Series

User Manual

Revision 3 (October 2013)

Legal and Regulatory Notices

Document History

maXis Series User Manual Revision 3 (October 2013)

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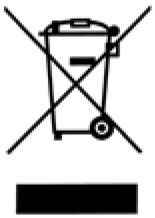


Under European Directive 2002/96/EC, this label applies to electrical and electronic equipment installed and sold in the European Union.

The consumer is committed by law to dispose of such equipment at the end of its lifetime. When disposing of the equipment or parts thereof, it must not be disposed of in household waste. To do so can contaminate and pollute the environment.

To dispose of the equipment responsibly, contact your community waste disposal authority. The details are regulated in national law.

Warnings

WARNING

Connecting an instrument to a power source that is not equipped with a protective earth contact creates a shock hazard for the operator and can damage the instrument. Likewise, interrupting the protective conductor inside or outside the instrument or disconnecting the protective earth terminal creates a shock hazard for the operator and can damage the instrument.

WARNING

It is not necessary to remove instrument covers except where specified in this manual as a customer maintenance activity. Only a Bruker Certified Engineer is permitted to remove covers other than those used for customer maintenance. Unless explicitly stated otherwise by this manual, the instrument must be switched off and disconnected from its power source before any cover is removed or opened. Bruker accepts no responsibility for loss or damage where this warning is ignored.

WARNING

All connections of the instrument must be used in correct way. The instrument should only be used with the wires and cables delivered with the system or otherwise provided by the manufacturer.

Instrument Identification

Each instrument is identified by a serial number. This numbers is located at the rear side of the instrument.

When corresponding with Bruker about your instrument, be sure to include the model name and the full serial number. Write the serial number of the instrument here for reference:

Instrument Serial #

Technical Support

If you encounter problems with your system please contact a Bruker representative in your area, or:

Bruker Daltonik GmbH
Fahrenheitstr. 4
28359 Bremen
Germany

Tel:	+49 421 2205 450
Fax:	+49 421 2205 370
E-mail:	esitof.support@bdal.de
E-mail (software support):	esi.sw.support@bdal.de
Internet:	www.bruker.com

Table of Contents

1 General

This manual provides an overview of the Bruker maXis Series system components and how they work together. This section deals with general topics mentioned throughout the manual.

1.1 Text Conventions

Throughout this manual, special fonts are used to differentiate instructions, commands, and button names from normal descriptive text:

- **Menu Options** and **Module** names are printed in **bold**.
- “Buttons” you click with the mouse are highlighted in quotation marks.
- ‘Group boxes’ are highlighted in apostrophes.
- *Filenames* are displayed in italic sans serif fonts.
- `otofControl commands` are written in courier font.
- Special keyboard keys are printed in bold courier font and within angle brackets, e.g., **`<ENTER>`**.

1.2 Site Preparation Specification

Before starting the installation of the instrument, the site must be properly prepared. Please refer to the maXis Series **Site Preparation Specification** document that is sent to all customers prior to the shipment of the instrument.

It contains information regarding the device requirements, such as operating environment, gas supply, power, exhaust, venting, grounding, etc.

This document has to be verified and returned to Bruker with the customer’s signature before a service representative will start the installation.

1.3 Safety

Safety considerations for the maXis Series spectrometer include:

- maXis Series Safety Symbols (section 1.3.1).
- Operating Precautions (section 1.3.2).
- Electrical Safety (section 1.3.3).

1.3.1 Safety Symbols

The following symbols may be found on or near various components of the mass spectrometer:

Table 1-1

Symbol	Description
~	Indicates that a terminal either receives or delivers alternating current or voltage.
⏚	Indicates that a protective grounding terminal must be connected to earth ground before any other electrical connections are made to the instrument.
O	Indicates the OFF position of the main power switch.
I	Indicates the ON position of the main power switch.

1.3.2 Operating Precautions

To protect yourself from harm and to prevent system malfunction, observe the following guidelines:

Before using the instrument, read all of the warnings explained at the beginning of this manual.

- Wear appropriate protective clothing, including safety glasses and gloves, when preparing samples and solutions for use with this instrument.
- Follow the correct safety procedure and the manufacturer's recommendations when using solvents. Read and follow precautions as detailed on the Material Safety Data Sheet (MSDS) obtainable from the supplier.
- Clean the exterior surfaces of the instrument with a soft cloth dampened with a mild detergent and water solution. Do not use abrasive cleaners or solvents.
- Exercise caution when moving as the maXis Series mass spectrometer as it weighs 345 kg / 760 lbs. Wear appropriate clothing and use appropriate equipment when carrying or moving the instrument.

CAUTION

Do not restrict the ventilation air intake or the exhaust, both located at the base of the instrument.

To ensure proper operation, check the ventilation air filters every three months. The ventilation filters are is situated in the base of the instrument and must be replaced if they becomes clogged.

Only use Bruker filter # 8216264 .

1.3.3 Safety

Safety considerations consist of the following sections:

- Before installing or operating the maXis Series mass spectrometer, read the following information concerning hazards and potential hazards. Ensure that anyone involved with installation and operation of the instrument is knowledgeable in both general safety practices for the laboratory and safety practices for the maXis Series mass spectrometer. Seek advice from your safety engineer, industrial hygienist, environmental engineer, or safety manager before installing and using the instrument.
- Position the maXis Series mass spectrometer in a clean area that is free of dust, smoke, vibration, and corrosive fumes, out of direct sunlight, and away from heating units, cooling units, and ducts.
- Verify that there is an adequate and stable power source for all system components.
- Verify that the power cord is the correct one for your laboratory and that it meets the national safety agency guidelines for the particular country of use.

WARNING

DO NOT attempt to make adjustments, replacements or repairs to this instrument. Only a Bruker Service Representative or similarly trained and authorized person should be permitted to service the instrument.

WARNING

The vent holes on the top of the instrument should never be covered under any conditions.

WARNING

When it is likely that the electrical protection of the maXis Series mass spectrometer has been impaired:

1. Power off the maXis Series mass spectrometer.
2. Disconnect the line cord from the electrical outlet.

Secure the instrument against any unauthorized operation.

WARNING

The maXis Series mass spectrometer uses very high voltages. Under normal operation, the instrument requires NO user access to the inner components of the instrument. NEVER operate the maXis Series mass spectrometer with the protective cover removed as this exposes the user to risk of severe electrical shock.

CAUTION

Use only fuses with the required current and voltage ratings and of the specified type for replacement.

CAUTION

Use the instrument according to the instructions provided in this manual. If abused, the built-in instrument protection may be impaired putting the operator at risk of serious injury.

CAUTION

Connect the instrument to an AC line power outlet that has a protective ground connection. To ensure satisfactory and safe operation of the instrument, it is essential that the protective ground conductor (the green / yellow lead) of the line power cord is connected to true electrical ground. Any interruption of the protective ground conductor, inside or outside the instrument, or disconnection of the protective ground terminal, can impair the built-in instrument protection.

1.3.4 CI-related Safety Precautions

If your instrument is equipped with a CI source for performing ETD reactions, several additional safety precautions apply.

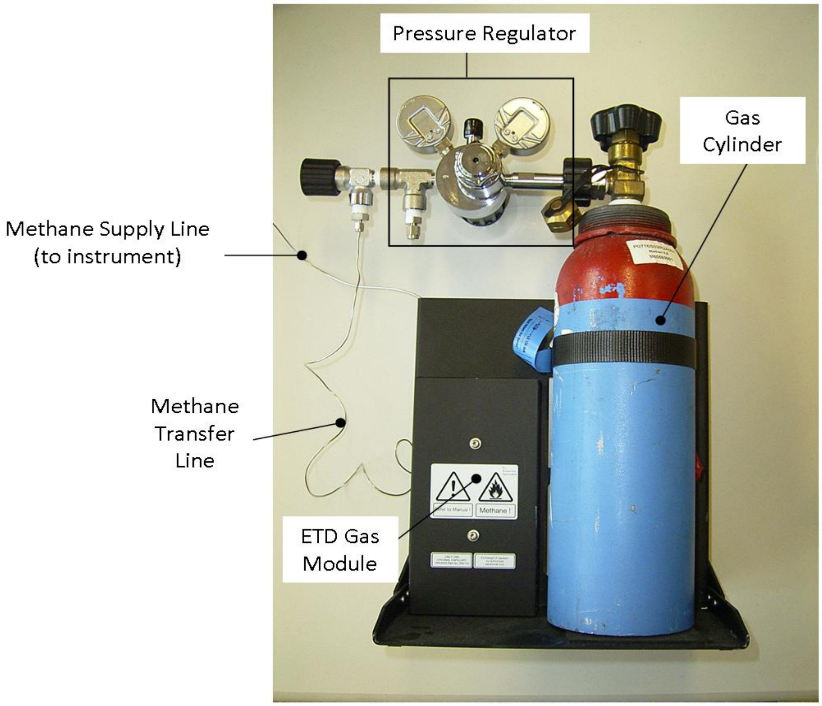


Figure 1-1 ETD Gas Module, methane gas cylinder, and pressure regulator

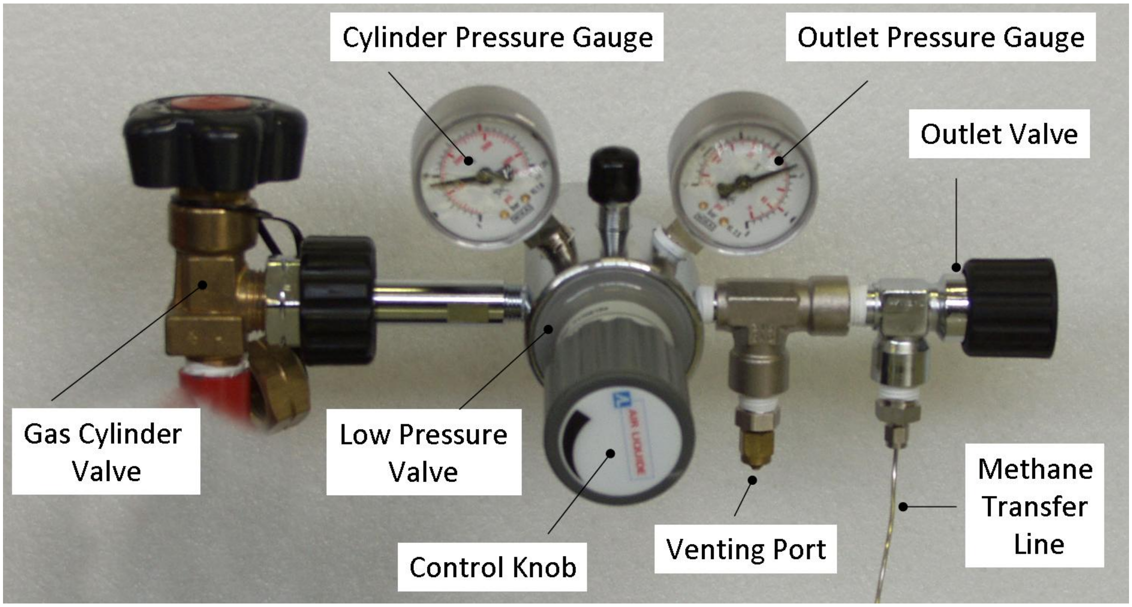


Figure 1-2 Typical methane two-stage pressure regulator

The components required for CI operation are:

- Methane gas cylinder. Maximum volume of 2 liters. Not supplied by Bruker. See the maXis Series Site Preparation Specification document for specifications.
- Pressure regulator. Not supplied by Bruker. See the Site Preparation document for specifications.
- ETD Gas Module (Bruker Part no. 8245568). Methane supplied from the methane gas cylinder and pressure regulator must pass through this module. To ensure safe operation, the ETD Gas Module must be used in conjunction with the instrument. Modification or customization of the ETD Gas Module is forbidden. In case of module failure, the entire module must be replaced. Contact your local Bruker representative for a replacement ETD Gas module.
- Methane Transfer Line (Bruker Part No. 8001931). This 1/16” capillary is used to connect the outlet valve of the pressure regulator to the ETD Gas Module inlet. It is connected to the outlet valve of the pressure regulator via a 1/16” Swagelok connector. Users should ensure that the outlet of their pressure regulator can accept this connection.

- Methane Supply Line. The Methane Supply Line is a 10 m connection capillary supplied by Bruker that is inserted between the ETD Gas Module and the instrument. Only methane supplied from the ETD Gas Module may be connected to the instrument.

- Methane Gas Flow Controller. This unit is supplied by Bruker and mounted to the vacuum chamber. It is not user accessible.

- CI Source. The CI source is supplied by Bruker and mounted to the maXis transfer cartridge in the vacuum system. This part becomes user accessible only in case of maintenance.

1.3.4.1 Precautions for Using Methane to Operate CI

The CI Source requires methane gas to function properly. Precautions are required to allow safe operation.

WARNING - FLAME AND EXPLOSIVE HAZARD

Methane is extremely flammable and can form explosive mixtures with air.

Keep containers in a well-ventilated area.

Keep away from ignition sources.

Take precautionary measures against static discharge.

- Methane is lighter than air and may accumulate beneath the ceiling of a room.

- The methane supply should always be closed when methane consumption is not required.

- Only use methane containers with volumes equal to or less than 2 liters (0.002 m^3) pressurized to 200 bar (400 bar L).

- The outlet pressure of the pressure regulator must be limited to a maximum of 4 bar.

- The ETD Gas Module limits the maximum methane flow-rate to not more than 0.5 L/h (0.0005 m^3/h) at 1 bar. This flow rate must not be exceeded.

- Gas cylinders must be kept in well-ventilated areas and well away from ignition sources (preferably in a gas cylinder cupboard). Refer to your national and local regulations.

- Keep container temperature below 50 °C.

- The ESI inlet capillary at the API source must not be blocked while the CI source is active. The nitrogen flow through the ESI inlet capillary must not be decreased in any way while the CI source is active.

- The installation of the methane supply and the installation of the instrument must be performed according to local regulations and to the requirements of the local facility safety representative.

- Use only properly specified equipment which is suitable for methane at this pressure and temperature.

- For safety reasons, the room in which the instrument is installed must have a size of at least 20 square meters. The height should be not less than 2.5 m.

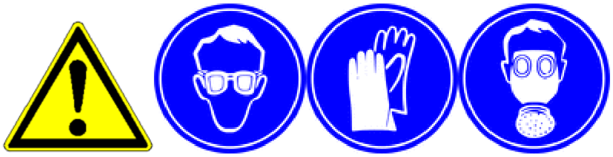
- An air exchange rate greater than 25 $m^3/m^2/h$ is recommended. The air exchange rate must not fall below 10 m^3/m^2 /h while the methane supply is opened.

- The methane supply line and the methane supply outlet pressure gauge must be evacuated in the following situations:
  - during installation,
  - after replacing a methane gas cylinder and
  - when the methane supply for the CI Source on this instrument is not used for extended periods.

- The methane supply line should also be checked periodically (at least every 3 months) for leaks. For this purpose the pressure gauge on the methane supply outlet must be able to indicate a pressure at least 1 bar below ambient pressure.

1.3.4.2 Reagent Precautions

WARNING



Always refer to a reagent's MSDS prior to handling it. Take appropriate precautions and wear appropriate safety clothing.

The CI source interface uses a reagent material to function properly. Refer to the reagent's MSDS for safety precautions. Pay attention to your local regulations!

The instrument vacuum pumps draw away the sample and solvent. The exhaust from these pumps can contain traces of your samples and solvents. Vent all pump exhaust outside the building or into a fume hood. Comply with your local air quality regulations.

1.3.5 Environmental Conditions

The maXis Series mass spectrometer is designed for indoor use and functions correctly under the following ambient conditions:

Table 1-2 Environmental Conditions

	Operating Conditions
Temperature	15 to 30 °C (56 to 86 °F)
Relative Humidity	15-85% non-condensing @ 30 °C

1.4 Facility and Electrical Requirements

The facility must provide:

Table 1-3 Power supply data

Region	Voltage
North America	208 VAC, ± 10% (dual phase voltage)
Europe	230 VAC, ± 10% (single phase voltage)
Australia	240 VAC, ±6% (single phase voltage)

- The instrument comes with a 3 m long IEC320 line cord and a mains plug, suitable for use in your country.
- The maXis Series mass spectrometer requires approximately 3.5m^2 of floor space including space for ventilation and access. The surface on which the maXis Series stands must be designed to safely support the full 345 kg (760 lbs) instrument weight.
- To ensure proper ventilation, and access to the connections and the main switch, maintain at least 500 mm (20 in) of free space on the left-hand side, 1000 mm (40 in) in front and 100 mm (4 in) behind the maXis Series.

WARNING

The main electrical supply must provide adequate grounding.

The system has an exhaust port to accommodate venting. This port is located at the rear of the instrument. Individual facilities may have safety guidelines, which require the exhaust gasses and particles to be treated in a particular way. It is the responsibility of each user to comply with the requirements of their respective facility.

1.5 Unpacking, Installation and First Setup

A packing list is created for each order and is placed in the crate with the equipment.

Note The warranty does NOT cover damage resulting from customer mishandling. Do not open the shipping container unless a BRUKER representative is present. Opening of the container without authorized persons will void the warranty of the instrument. Our service engineers will set up the instrument in the customer's laboratory.

The surface on which the instrument is to be located must be able to safely support the full 345 kg (760 lbs) weight. In addition tables or benches will be required to set up the LC-unit, the computer, monitor and printer. It is recommended that the table height should be between 23 and 28 inches (58 to 71 cm).

Once delivered, the machine must remain on the delivery palette in readiness for a Bruker representative to move the instrument to its desired location.

Please note: Only a Bruker representative is permitted to undertake the initial installation and commissioning of the maXis Series.

2 Identifying System Components

This chapter is an overview of the maXis Series and gives a short theory explanation.

2.1 Overview

The Bruker maXis Series is a Hybrid Quadrupole / Atmospheric Pressure Ionization orthogonal accelerated Time-Of-Flight mass spectrometer.

It is a space-saving reflector instrument configured with the Bruker Apollo ion source, an analytical quadrupole and a vertically arranged ion flight tube that contains the orthogonal acceleration stage, the reflector, and a detector. The PC mounted digitizer is able to attain a sample rate up to 4 GS/sec.

Figure 2-1 illustrates the dimensions of the instrument.

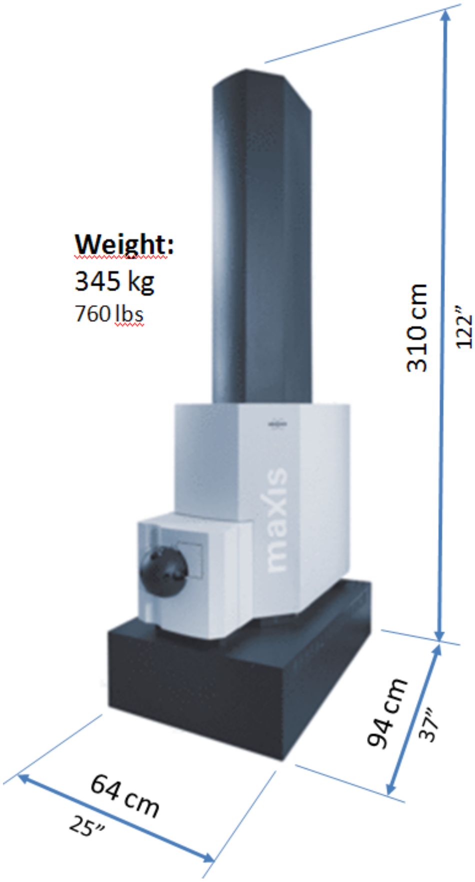


Figure 2-1 maXis Series weight and dimensions

Figure 2-2 shows the maXis Series in a typical LC/MS/MS arrangement. For details about the liquid chromatographic system or the syringe pump see the manual supplied with those delivery systems.

Figure 2-2 Example of an LC/MS system arrangement

It is a space-saving instrument, which includes the Apollo II Electrospray Ion Source, a quadrupole MS/MS-stage, a vertically arranged Time of Flight mass spectrometer, a vacuum system (including the rough pump) and complete electronics.

Included with the maXis Series there is the data system (PC) and a syringe pump for both low-flow and high-flow direct infusion work. The PC incorporates a fast digitizer for data acquisition. The “Compass” software includes “**otofControl**” for instrument control and data acquisition, “**DataAnalysis**” for data post processing and “**HyStar**” which provides full automation of LC/MS workflow.

The maXis Series is a time-of-flight instrument used in combination with LC/MS/MS applications. Sample delivery to the source is generally either by a syringe pump or HPLC[1] system (Figure 2-2 and Figure 2-4). If the mass spectrometer runs in combination with an offline-nanospray-source, no external sample delivery device is required, as the solved sample is manually placed into a specific position in the source.

The HPLC may contain a column to perform a “pre-separation” of sample compounds before they enter the mass spectrometer.

This combination of HPLC and MS allows for the detection of masses in a complex matrix. LC/MS can be used for analytes that do not have chromophores, and is considered a highly selective and sensitive technique.

Figure 2-2 shows the mass spectrometer with its atmospheric pressure interface (API) and the Liquid Chromatographic System. The PC, the rough pump and the syringe pump are not shown here.

[1] *HPLC (High Performance Liquid Chromatography)*

2.2 Sample Input Devices

Samples can be introduced into the mass spectrometer through a variety of delivery systems. Each system is designed to deliver a particular flow rate and is used for specific applications. See www.bruker.com for more information about additional Bruker ion sources.

The following sample delivery systems can be used with the supplied API source:

• Liquid chromatographic system

(10 mL/min – 1000 mL/min; max 5000 mL/min)

• Syringe pump

(0.3 mL/min - 10 mL/min alone and 100 mL/min –1000 mL/min with LC pump;

max 5000 mL/min)

• Divert valve introduction

directs the sample either to the source or via the bypass to waste

2.2.1 HPLC system

Due to the widespread use of liquid chromatography, the LC-system is the most common form of sample delivery for the instrument. The electrospray ionization is optimized to accept flow rates up to 1 mL/min and with the APCI option flow rates up to 1.5 mL/min are possible. The nebulization process for both of these ion sources is assisted with nebulizing gas and countercurrent drying gas.

The LC system can be operated in several modes in conjunction with the instrument. Normal modes include standard LC analysis, analysis without LC separation (flow injection analysis, FIA) and combined flow with the low flow syringe pump. The LC-System may contain a column to perform a “pre-separation” of sample compounds before they enter the mass spectrometer.

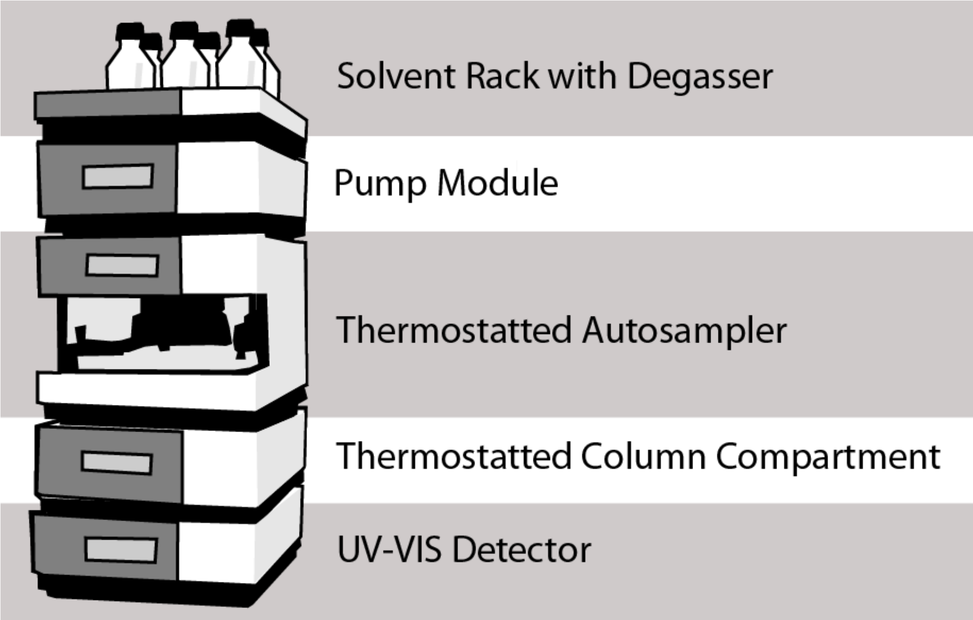


Figure 2-3 Typical LC System

2.2.2 Syringe pump

A small syringe pump (see Figure 2-4) is included with the maXis Series system to facilitate the introduction of samples directly into either the electrospray or APCI ion sources.

The syringe pump is supplied with a 250 µL syringe. Smaller and larger syringes can also be used.

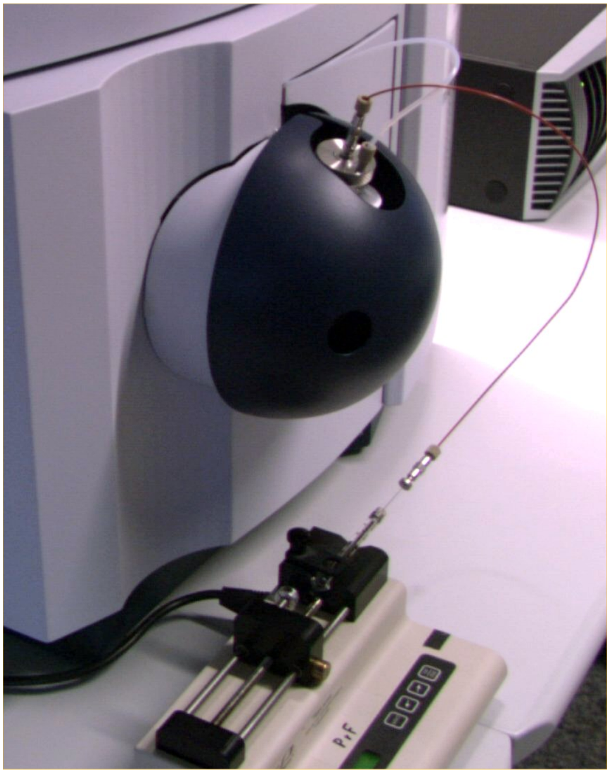


Figure 2-4 Syringe pump coupled to the Apollo source

When used with electrospray ionization, two modes of operation are available. Either the syringe pump can deliver the sample in solution directly to the nebulizer under low flow conditions (typically 1 µL/min – 10 µL/min) or it can supply a small flow that is tee'd into the flow from an LC system. This combined operation is particularly convenient for the optimization of instrument parameters and the development of MS/MS methods. The syringe pump / LC delivery approach is recommended for APCI. This is because the APCI ion source is designed for a minimum flow rate of approximately 100 µL/min.

2.2.3 Divert Valve Introduction

The divert valve allows the sample to bypass the ion source preventing contamination of the ion source and the vacuum system.

Selecting “To Source” lets the sample pass through the valve to enter the source (default); selecting “To Waste” switches the valve so that the sample flows directly into a drain bottle (useful for a large solvent peak and a small compound peak to direct the solvent peak to waste, or to reduce memory effects after using samples which may contaminate the source).

Another application is to use the standard 20 µL sample loop to inject a calibrant after a measurement for example. A detailed explanation of the divert valve can be found in (see section A.3).

otofControl allows eluent to be directed either into the ion source or to waste via the divert valve.

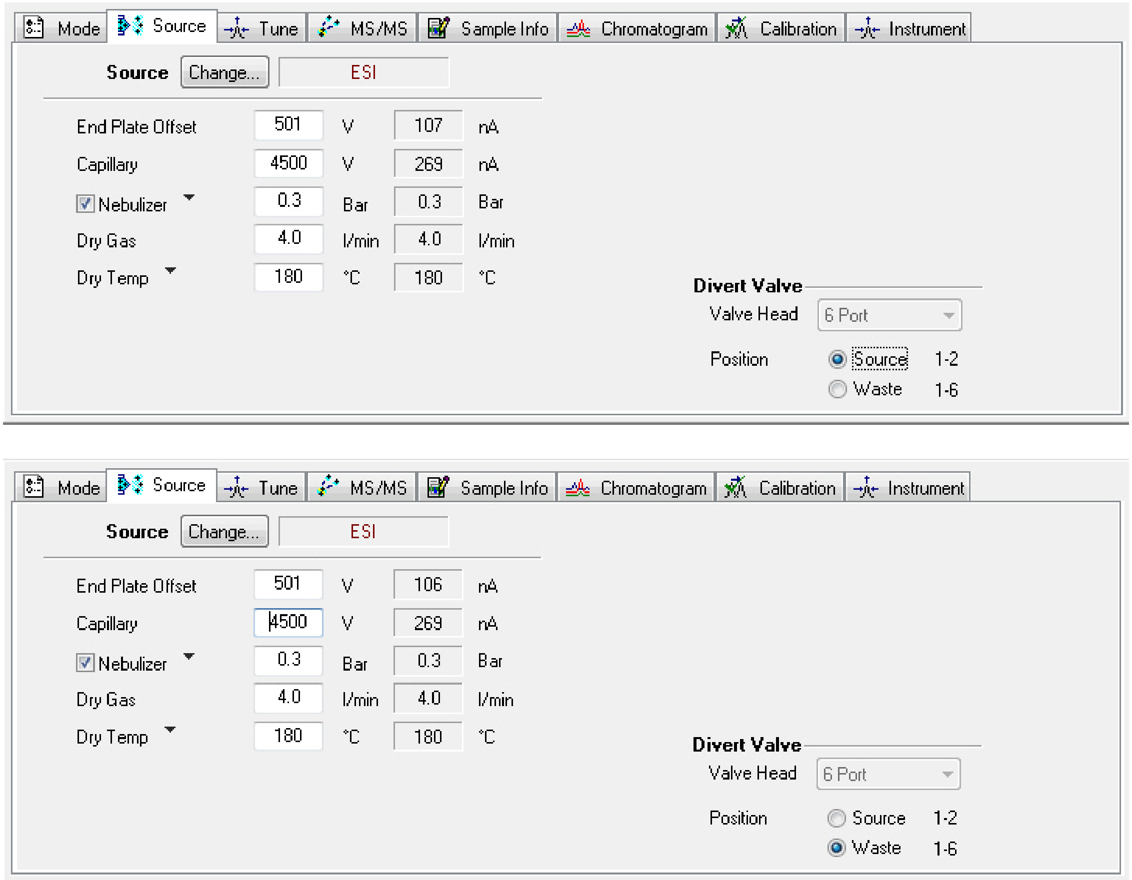


Figure 2-5 Top: Sample to source; Bottom: Sample to waste

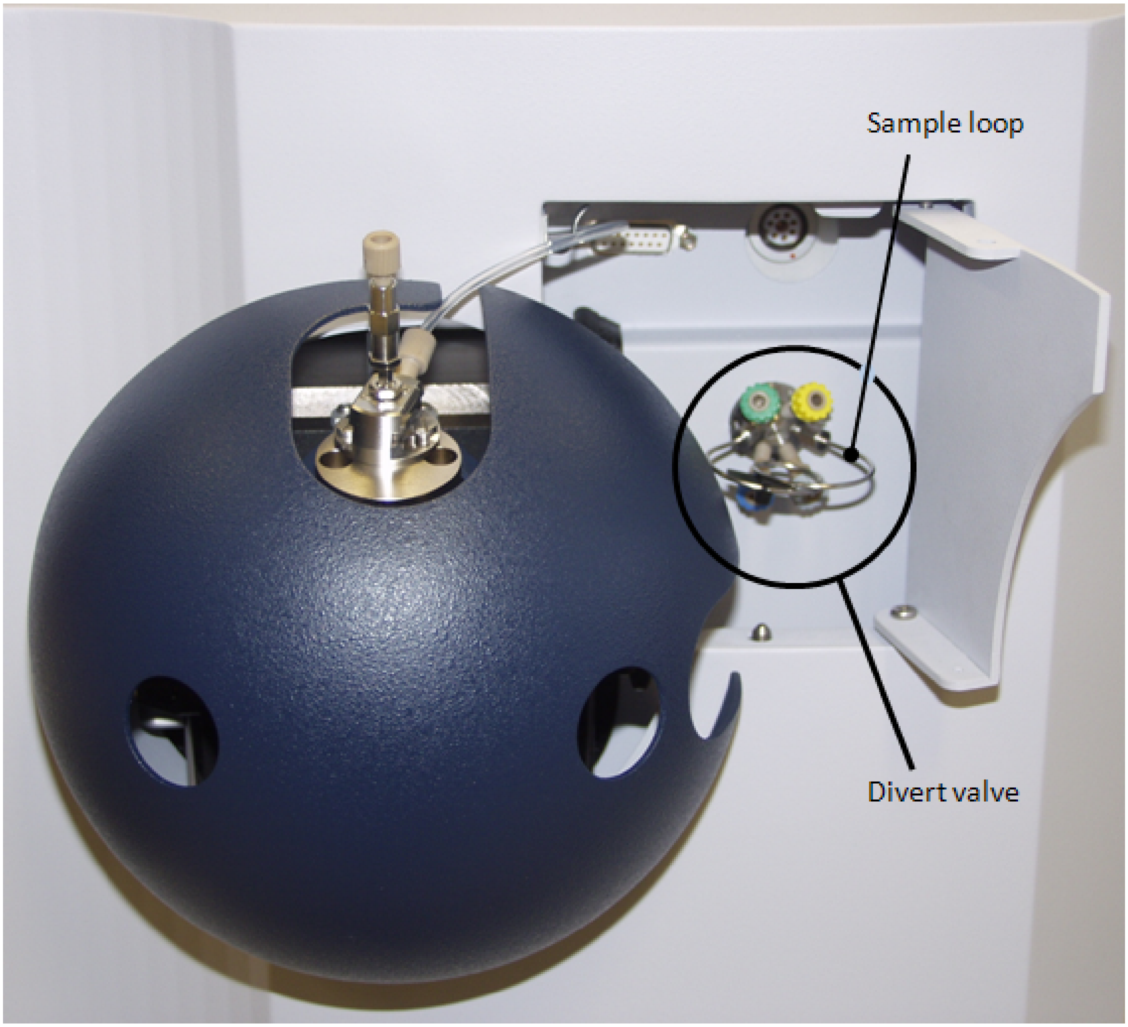


Figure 2-6 Front view of the maXis Series showing Divert Valve fitted with sample loop

2.3 Route through the TOF-Mass Spectrometer

maXis

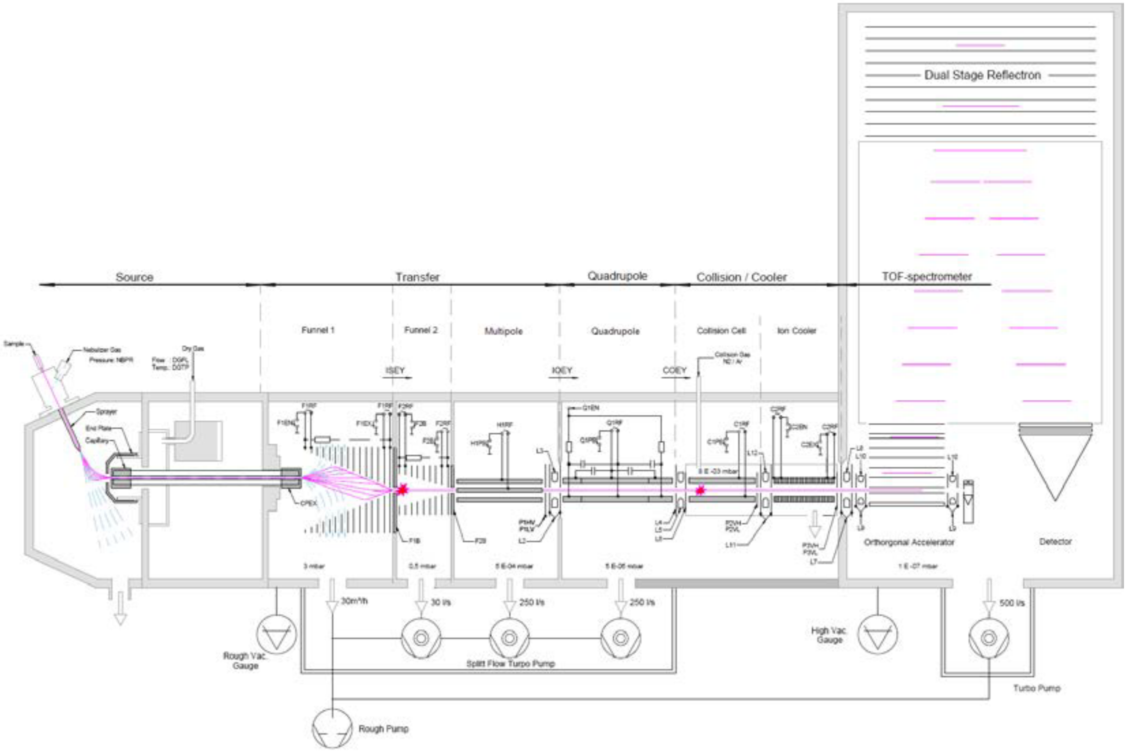


Figure 2-7 **Source (spray chamber and capillary), Ion Transfer Stage (funnel 1, funnel 2 , multipole), Quadrupole, Collision/Cooling Cell and TOF spectrometer (orthogonal accelerator, dual stage reflector, detector)**

maXis ETD

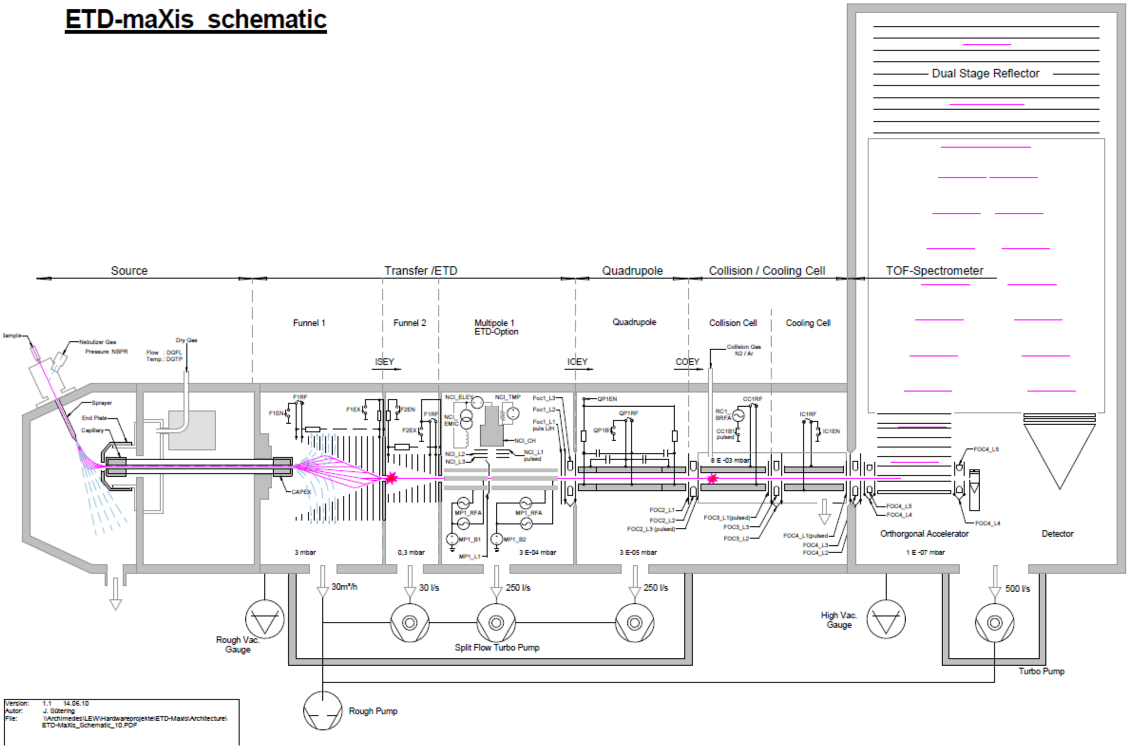


Figure 2-8 Source (spray chamber and capillary), Ion Transfer Stage (funnel 1, funnel 2 , multipole), Quadrupole, Collision/Cooling Cell and TOF spectrometer (orthogonal accelerator, dual stage reflector, detector)

maXis HD ETD

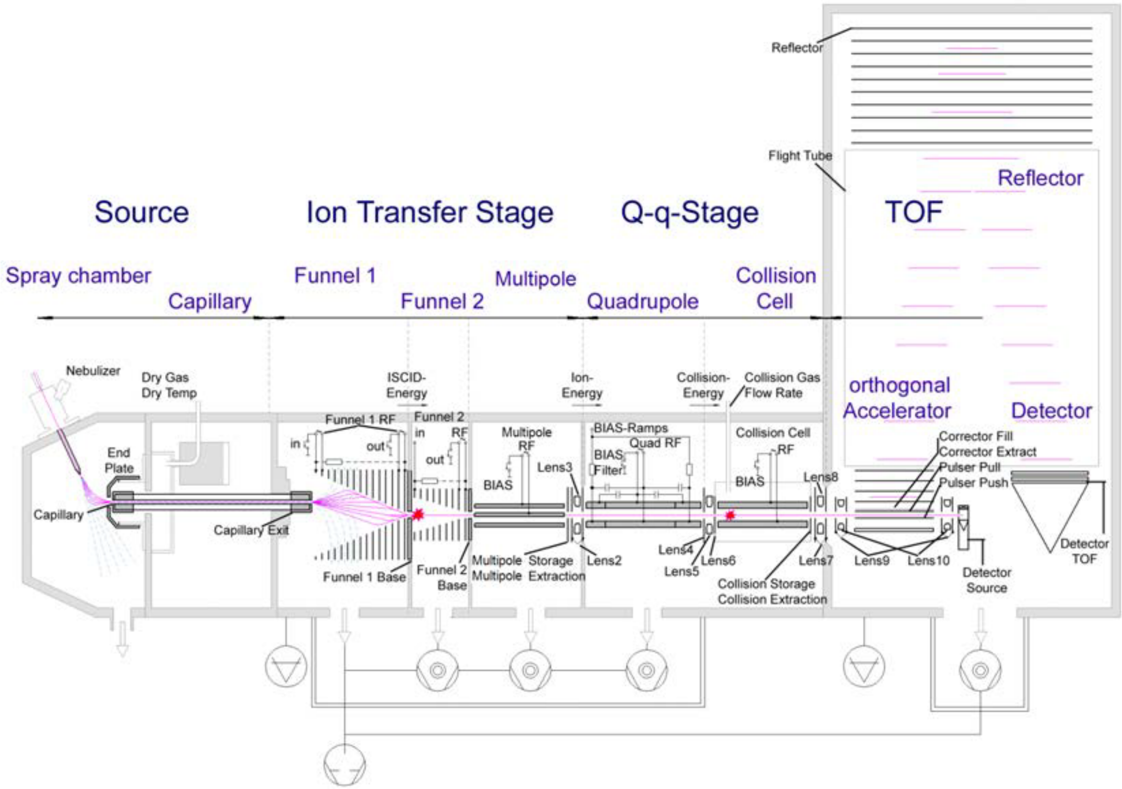


Figure 2-9 **Source (spray chamber and capillary), Ion Transfer Stage (funnel 1, funnel 2 , multipole), Quadrupole, Collision/Cooling Cell and TOF spectrometer (orthogonal accelerator, dual stage reflector, detector)**

2.3.1 Apollo Source (ESI)

The Bruker Apollo-source (Figure 2-10) is the standard ion source used with the maXis Series for the measurements of singly charged samples such as benzodiazepines, and multiple charged samples such as proteins, and peptides.

The solved sample is introduced through the nebulizer assembly into the spray chamber, where it is subjected to the ESI process by means of an electrical field between the inner chamber wall and the spray shield, and with the aid of a nebulizer gas (N_2).

Heated drying gas (N_2), flowing in the opposite direction to the stream of droplets, enters the spray chamber, and is used to aid volatilization, thus ionization, and to carry away any uncharged material. The desolvation assembly (section 2.3.1.5) delivers the pressurized drying gas and guides it past the spray shield into the spray chamber at temperatures ranging from 120 °C to 365 °C, and flowing at a rate of between 1 and 12 l/min.

Ions are attracted by the electrical field strength between the spray chamber (ground potential) and the negatively biased metal-coated glass capillary, the inlet to the vacuum system. A potential difference of ~400 V between the spray shield and the tip of the glass capillary acts as a further ion pull into the vacuum system.

All flows, temperatures and bias voltages are adjusted and controlled automatically by the data system (please refer to the otofControl manual).

The waste pipe of the spray chamber, used to pump away solvents, gas and sample molecules, is connected to the rough pump. The door of the spray chamber can be opened for maintenance purposes. On opening this, an interlock switch isolates all high voltages to the spray shield and capillary cap.

Functionally the interface consists of the following components:

1. Spray chamber
    - Nebulizer (-gas)
    - Spray shield
    - Capillary cap
    - Drying gas
    - Desolvation unit with:
        - Glass capillary
        - Dry gas heater

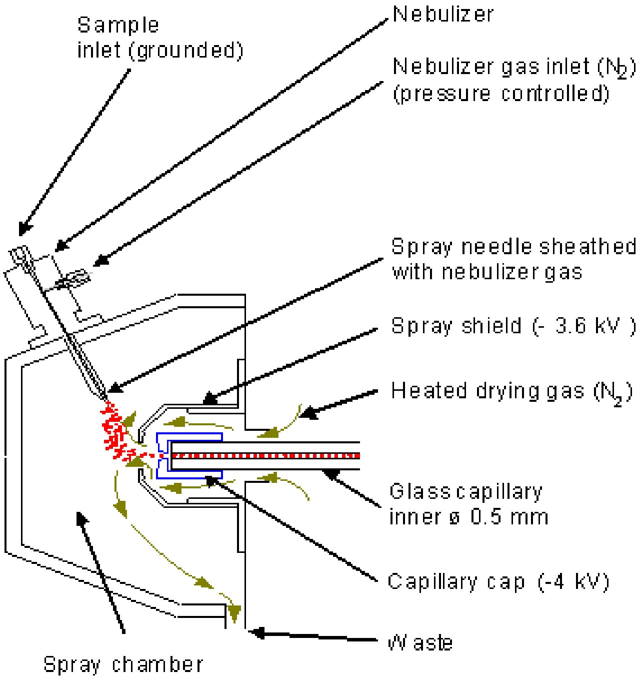


Figure 2-10 Schematic of an APCI interface

2.3.1.1 Nebulizer

To achieve reasonable sensitivity in the mass analysis of liquid samples, the solved sample must first be sprayed into very fine droplets, which can be easily evaporated prior to entering the vacuum system. This is best achieved with the use of a pneumatic nebulizer which routinely produces droplets within a controlled range.

The nebulizer (see Figure 2-10) receives the solution of sample and solvent from a syringe pump or liquid chromatograph. The solution passes through a very fine needle. The needle is mounted inside a tube that transports pressurized nebulizer gas (usually nitrogen). At the end of the tubes the two streams interact in such a way that the solution is dispersed into small droplets.

The nebulizing gas is important for the production of a good spray and a steady ion stream. The operator can manually adjust the position (extension) of the needle, although this is not normally necessary. The pressure of the nebulizing gas is controlled by the user through the data system to optimize the spray. The presence of the electrospray can easily be checked through a viewing window in the spray chamber. The needle assembly is electrically grounded.

2.3.1.2 Electrospray

Electrospray describes the dispersion of a liquid into many small charged droplets as a result of an electrostatic field. In the early seventies, initial experiments were conducted with oligomers dissolved in a volatile solvent, which were guided through a N_2 sprayer into a cell filled with N_2. Dispersion was initialized by the application of a potential of some 1000 volts between the sprayer and shield (Figure 2-11).

Evaporation of the solvent during this process result in the droplets reduced in size and causes a buildup of charge density on their surface, finally resulting in coulombic forces, which break up the droplets further. This process is repeated until final desolvation [1] generates sample ions, as shown in Figure 2-11.

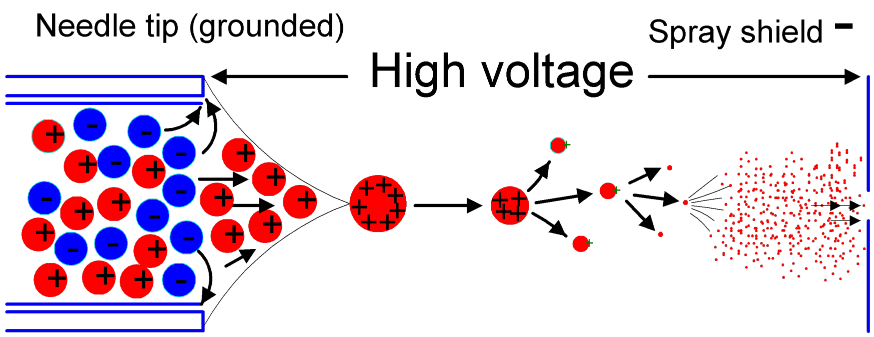


Figure 2-11 Principle of the ESI process

[1] *Transfer of ions from the solvent into the gas phase.*

2.3.1.3 Spray shield and capillary cap

A high voltage is applied to the spray shield to attract the ions. The small charged droplets generated by the nebulizer are accelerated by the electrical field between the nebulizer (ground potential) and, in the case of positive charged droplets, the negatively charged spray shield. A further potential difference of about -500 V between the spray shield and the capillary cap focuses the ions directly onto the entrance of the glass capillary.

2.3.1.4 Drying gas

The drying gas, usually nitrogen, is used to completely evaporate the solvent in the small droplets before they enter the capillary. The drying gas streams through the opening in the spray shield against the flow of the charged droplets in the spray chamber (see Figure 2-10).

The gas is typically heated to between 100 °C and 350 °C at a flow rate of between 1 l/min and 12 l/min. Flow and temperature are controlled by the data system and have to be adapted for each application. While the drying gas assists in the desolvation process it does not thermally decompose the analytes.

2.3.1.5 Desolvation Unit

Basically the **desolvation unit** (see Figure 2-12) includes the drying gas heater, the guidance of the heated drying gas, the electrical connectors for the ESI high voltages and the glass capillary.

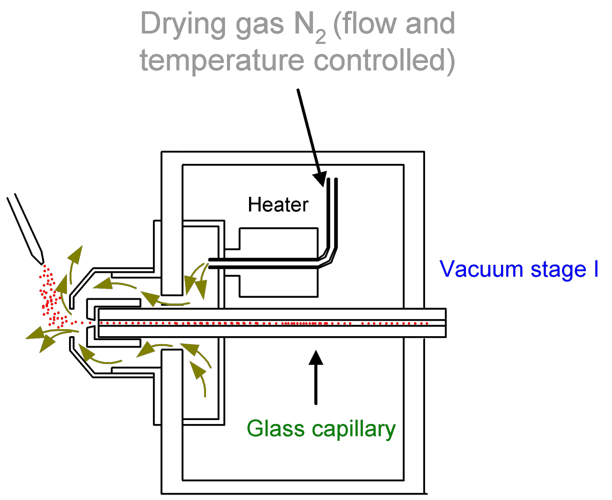


Figure 2-12 Desolvation unit

The analyte ions are transferred through the glass capillary from the spray chamber into the first stage of the vacuum system. The inner diameter and the length of the capillary determines the gas flow and so the pressure in the first vacuum stage.

The second function of the glass capillary is to isolate the high voltages at the entrance to the capillary (see above) from the low voltages needed at the end of the capillary for the subsequent ion optics (see 2.3.2).

In the drying gas heater, pressurized nitrogen is heated up to a pre-defined temperature. the drying gas streams Through a heat chamber and around the capillary from the rear of the spray shield.

2.3.2 Ion Transfer stage

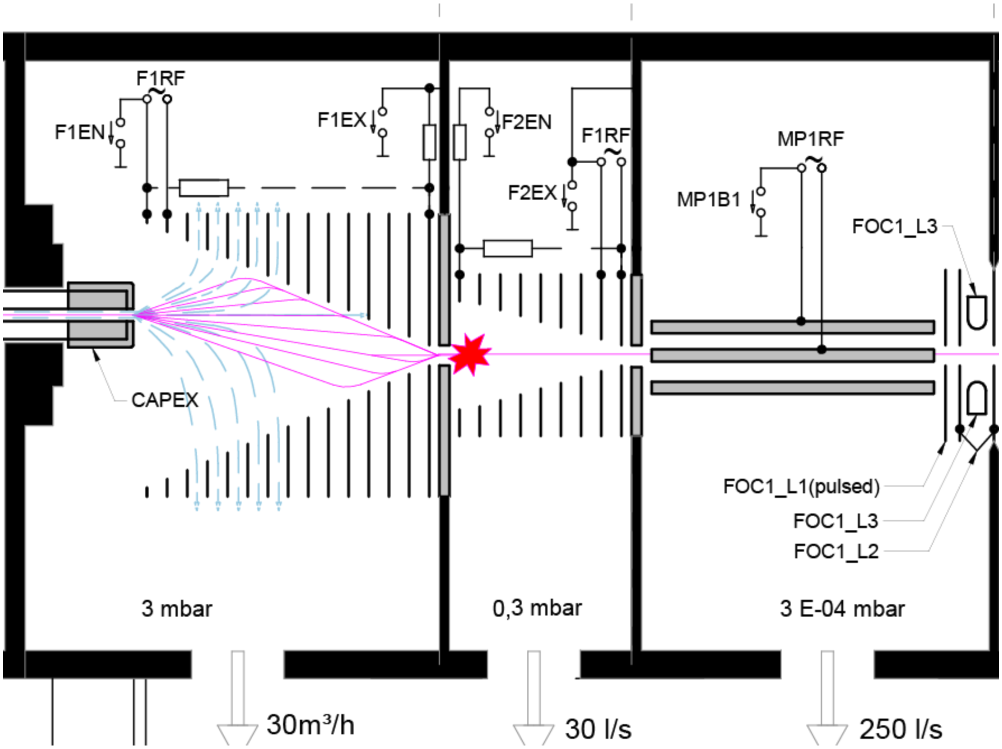


Figure 2-13 Double Stage Ion Funnel and Multipole

2.3.2.1 Double Stage Ion Funnel

The ion transfer stage (Figure 2-13) contains the first three of the five vacuum stages in the maXis Series mass spectrometer. The glass capillary transmits analyte ions, drying gas and a small amount of solvent into the vacuum system. The first stage is pumped by a 28 m^3 roughing pump, which reduces the pressure to approximately 3 mbar. The aim of the ion transfer region is to separate analyte ions from drying gas and solvent and to transfer these ions, with minimal losses, to the quadrupole stage, which requires a pressure lower than $3x10^{-5}$ mbar.

The first two vacuum stages of the ion transfer contain funnel ion guides. These are stacked ring ion guides with the inner profile of a funnel. The applied RF voltage generates an effective potential that confines the ion beam inside the funnel. Two DC-voltages connected to the first and last plate of the funnel direct the ions towards the funnel exit using an adjustable DC-gradient.

The wide opening of the funnel 1 entrance collects nearly all the entering ions without the need for a strong focusing electrostatic field. For this reason the funnel configuration has a high transmission efficiency especially regarding fragile analyte ions. The small inner diameter of the funnel plates at the funnel 1 exit ensures a well defined ion beam near the axis of funnel 1. Uncharged particles like drying gas will be pumped away through the gaps between the funnel plates. To avoid contamination at the funnel 1 exit and the following ion optics, the funnel axis is offset from the capillary axis. Small droplets entering this stage will hit the outer funnel plates, while the offset-axis configuration has no negative effect the ion transmission.

The first and second funnel stages are separated by a DC plate. This is F1 base. The diameter of the orifice restricts the gas flow into the next stage. The funnel 2 stage is connected to the intermediate stage of a triple stage turbo pump (Figure 2-8). Ion Transfer stage The operating pressure is $3x10^{-1}$ mbar.

By increasing the DC potentials of funnel 1 the ions will be accelerated into the funnel 2 stage. This fact can be utilized to activate **I**n **S**ource **C**ollision **I**nduced **D**issociation (ISCID).

2.3.2.2 Multipole Transfer Stage and CI Ion Source

After exiting the second ion funnel through a small aperture, ions enter the subsequent differential pumping stage. Here, ions are guided using a high-precision multipole.

The Bruker patented wire-eroded multipole setup guarantees optimal ion transfer. The applied RF voltage generates a radially increasing effective potential, so that the ions are focused onto the multipole axis. The multipole stage ends with a gate lens and a focusing lens assembly.

In the maXis Series instrument, this stage of the ion transfer is equipped with a CI ion source that allows direct coupling of reagents for ion/ion reactions into the main ion optical path. This enables the robust and easy use of ETD ion/ion reactions. Reagent anions for ETD are generated in a negative chemical ionization (CI) source mounted perpendicularly to the multipolar transfer optics.

For fragmentation of peptides via electron transfer dissociation, an excess of radical anions is extracted out of the negative chemical ionization (CI) source and added to multiply charged peptide cations that have previously been stored in the reaction cell (see Figure 2-14). The electron transfer from the reagent anion to the analyte cation locally disturbs the peptide backbone leading to N-Cα bond cleavage and finally produces c- and z-type fragment ions.

In contrast to CID, ETD has no mass bias. The electron transfer reaction generally occurs independent of m/z range but it is strongly related to the charge state. Multiply charged ions will react much faster and, as a first approximation, the speed is related to the square of the charge. Therefore, a mixture of non-isolated peptides will produce fragments that predominantly originate from the most highly charged precursor ions.

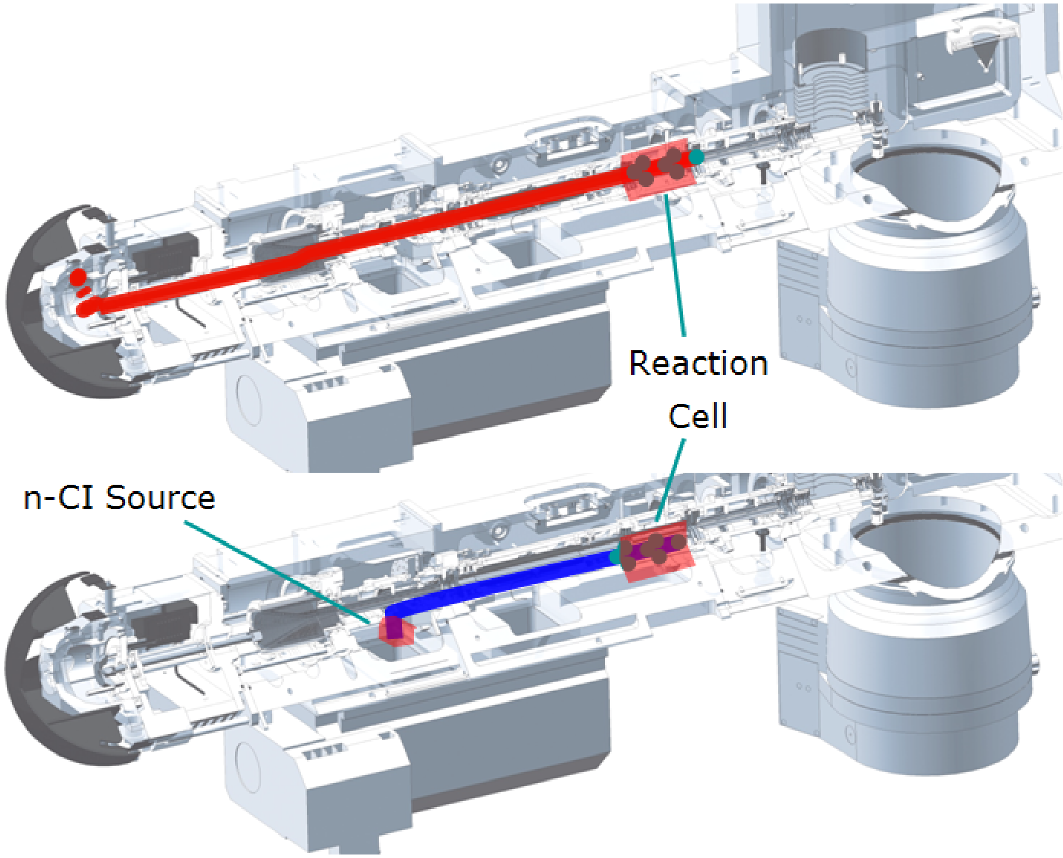


Figure 2-14 CI source function principle shown for an ETD experiment

2.3.3 Quadrupole

The analytical quadrupole is located in the fourth pumping stage of the vacuum system. The second turbo stage of the triple stage turbo pump reduces the pressure down to approximately $3x10^{-5}$ mbar.

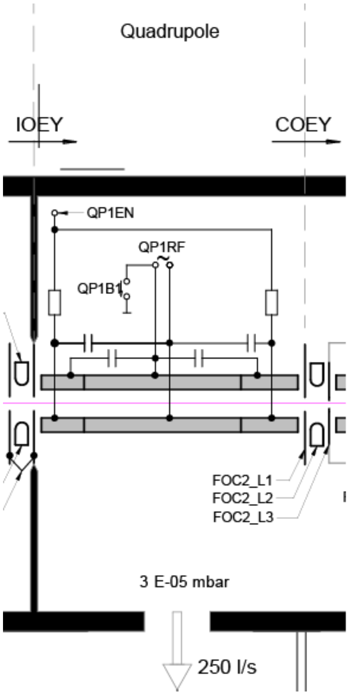


Figure 2-15 Quadrupole

The analytical quadrupole is the first mass analyzer in the maXis Series. It is used as a mass filter to isolate a certain ion mass or a defined mass range. The isolation width is adjustable from 0.1 to 300 Dalton. For MS analysis the resolving power of the quadrupole can be switched off. In this case the quadrupole works as an additional ion guide.

The analytical quadrupole consists of three quadrupole segments. The middle segment is the resolving part of the mass filter; the outer segments optimize the ion transfer efficiency if the quadrupole is used as a mass filter. The same RF-voltage is applied to all segments. The bias voltage can be selected separately for the middle and the outer segments. To achieve the resolving power, the RF voltage of the middle element is superimposed with an asymmetric DC-voltage. For a detailed explanation of the functionality of a quadrupole mass filter (see section 4).

With the Q-q-stage (Figure 2-16) consisting of an analytical quadrupole and a collision cell the hybrid maXis Series achieves the capability to isolate and fragment parent ions prior to mass analysis with the TOF-mass spectrometer.

2.3.4 Collision Cell / Cooling Cell

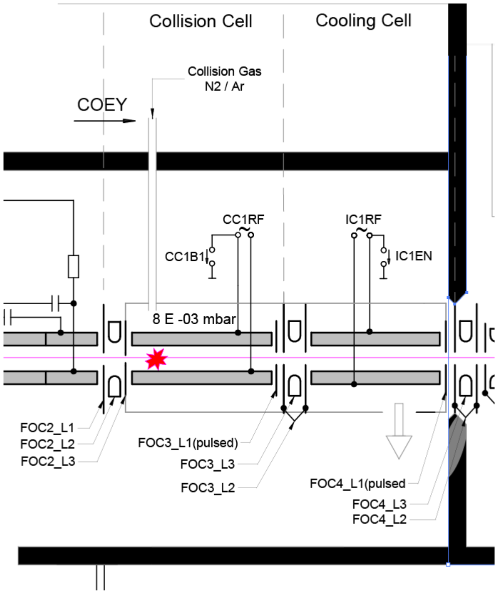


Figure 2-16 Collision Cell / Cooling Cell

2.3.4.1 Collision Cell / Reaction Cell

In the collision cell the isolated parent masses can be fragmented by **C**ollision **I**nduced **D**issociation (CID). For this purpose a neutral collision gas, typically nitrogen or argon, is introduced at about 10^{-2} mbar.

A hexapole is used to guide and focus the parent ions and the fragment-ions. To maintain the high vacuum conditions in vacuum stage 4 the hexapole is enclosed in a chamber (the collision cell) with small apertures at the entrance and exit. A lens is needed to focus the ion beam on the small entrance aperture in front of the collision cell. To obtain optimal fragmentation efficiency the collision energy can be adjusted by increasing all DC voltages in front of the collision cell (ion transfer stage and quadrupole mass filter) up to 200 eV. Due to the high pressure inside the collision cell and the effective potential generated by the hexapole RF field, the ions cool down (lose their energy) and can be focused very tightly onto the axis of the collision cell.

2.3.5 HD Collision Cell

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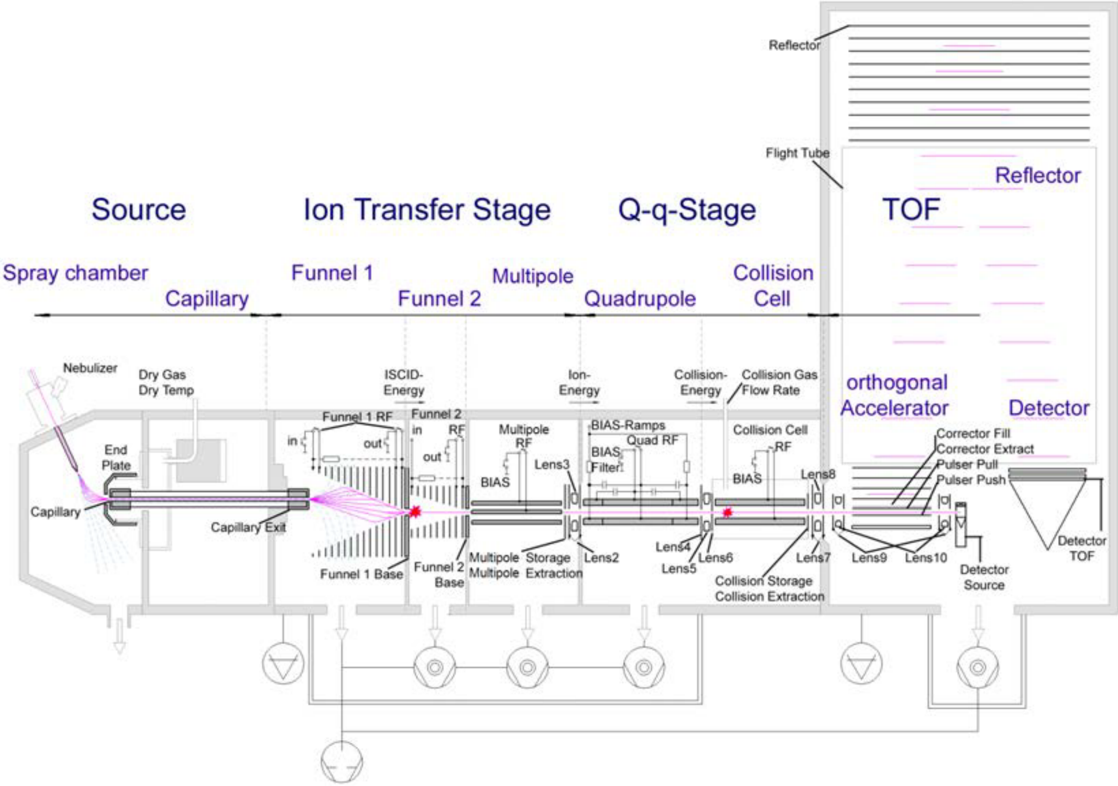

In the HD collision cell the isolated parent masses can be fragmented by Collision Induced Dissociation (CID). For this purpose a neutral collision gas, typically nitrogen or argon, is introduced at about 10^{-2} mbar.

A multipole is used to guide and focus the parent and the fragment-ions. To ensure the high vacuum conditions in vacuum stage 4 the quadrupole is enclosed in a chamber (collision cell) with small apertures at the entrance and exit. A lens focuses the ion beam on the small entrance aperture in front of the collision cell.

To obtain optimal fragmentation efficiency, the collision energy can be adjusted by increasing all DC voltages in front of the collision cell (ion transfer stage and quadrupole mass filter) up to 200 eV.

Due to the high pressure inside the collision cell and the effective potential generated by the quadrupole RF field, the ions cool down (lose their energy) and will be focused very tightly onto the axis of the collision cell.

The collision cell for maXis HD, maXis plus and maXis instruments is upgraded with the HDC-cell and ends with a gate lens and a transfer lens. During the fragmentation of parent ions the gate and lens voltages are set to block ion transmission to the TOF stage.

This facilitates the efficient accumulation of fragment ions. After an adjustable time slot, the voltage is set to transfer the accumulated ions into the TOF-stage. The **Transfer Time** defines the beginning of the time slot and the **Pre Pulse Storage Time** defines the end of the time slot. Both are referenced to the next TOF-pulse and limit the transferred mass range.

A higher µs value for **Transfer Time** will give a higher upper limit of transferred m/z . A lower µs value for **Pre Pulse Storage Time** will reduce the lower limit of transferred m/z. The transfer lens combines with the entrance lens of the orthogonal accelerator to generate a suitable parallel beam shape inside the acceleration stage.

2.3.6 TOF Assembly

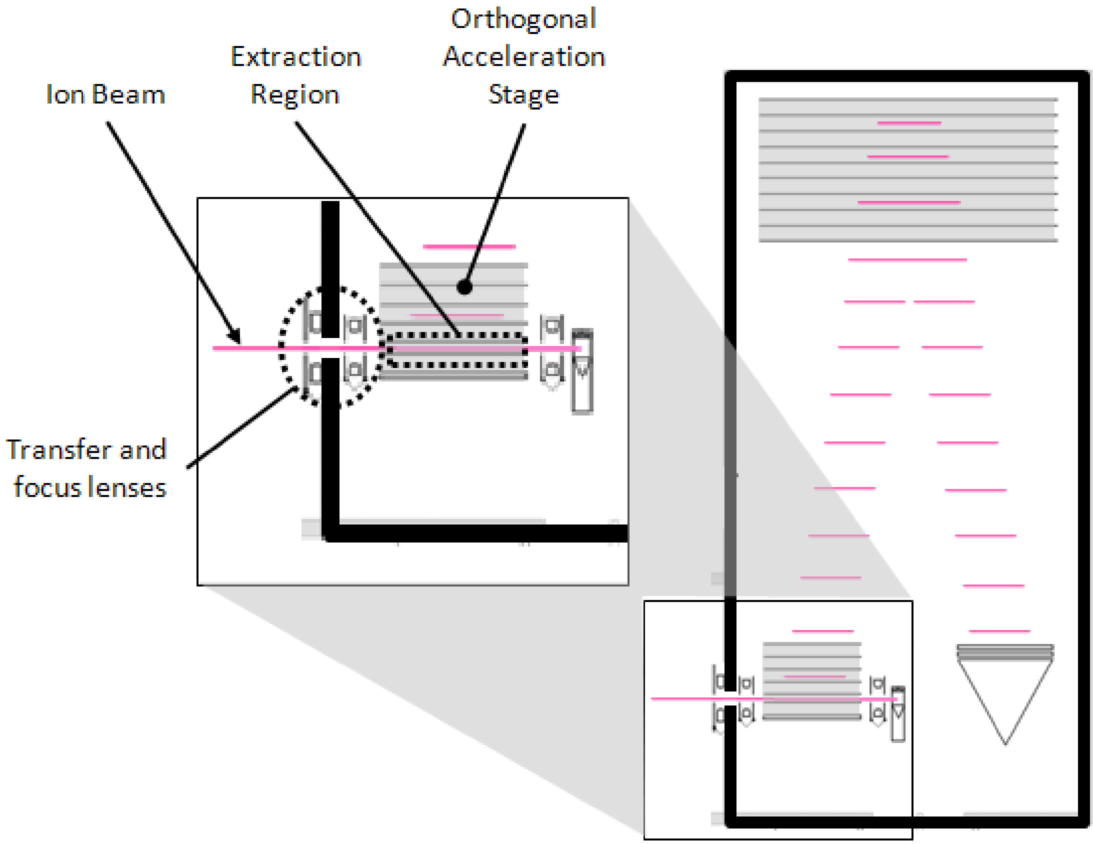

Figure 2-17 Schematic of the TOF assembly

The layout of the TOF assembly is shown in Figure 2-15. The main components of the TOF assembly are:

• Orthogonal acceleration stage (see section 2.3.6.1)).

• Reflector (see section 2.3.6.4).

• Detector (see section 2.3.6.5).

In ESI-TOF applications the orthogonal acceleration stage replaces the ion source. This stage does not create ions, but simply deflects and transfers incoming ions to the reflector by the use of pulsed voltages.

During pulser off time, when electrodes of the acceleration stage are maintained at ground potential, the incoming ion beam is guided directly to the conversion dynode of the SEM (Secondary Electron Multiplier) (Figure 2 15Figure 2 15). This set-up is used for monitoring ions, and can be used for troubleshooting or tuning the ESI-System. This detector is not used to acquire spectra!

2.3.6.1 Orthogonal Acceleration (Pulser)

In the maXis Series the orthogonal acceleration stage represents the ion source normally operating in pulsed mode. This assembly consists of an array of electrodes mounted on top of one another. Excluding the base electrode, all the others assembled towards the reflector are shaped like slot diaphragms. This region is used to accelerate ions towards the reflector.

Orthogonal acceleration on the maXis Series is a two-stage process:

If the acceleration electrodes are at ground potential the incoming flow fills this region with ions, which continue straight ahead to the SEM dynode. Ions that have passed out of the pulsing region are not available for TOF analysis.

Before ions leave the pulsing region appropriate voltages are applied to the acceleration electrodes. The ion package in the pulsing region is now forced to pass through slits of the electrodes towards the reflector. This fill, cut-off, and acceleration process can be repeated up to 20,000 times / second.

Before the continuous flowing ion beam has re-filled the pulsing region, to be sampled again and accelerated, the previous ion package has just reached the reflector and detector.

The link between pulser fill time and TOF pulse time allows an ion loss of about 5%.

2.3.6.2 HV Focus Lens

The HV Focus Lens is part of the orthogonal acceleration stage. Due to the long flight path of the maXis Series it is necessary to focus the ion beam with great precision to ensure a high ion yield at the detector. The HV Focus Lens is a lens system that focuses the ion beam during the acceleration phase to reduce beam divergence and optimize utilization of the detector surface.

2.3.6.3 Determination of the m/z Ratio

Charged ions are not detected by their mass alone but by their mass-to-charge ratio, m/z. m/z is used to scale the x axis of mass spectra.

The charge state of an ion has influence on its behavior in the mass analyzer.

Ions with *n* charges are detected at a 1/*n* mass scale, e.g., mass = 1000 amu with two charges is detected at m/z 500. This is true for all types of MS. Isotopic peaks of *n* times charged ions are at 1/*n* amu distance. This allows an easy identification of the charge state from isotopically resolved spectra, which is of high importance for ESI spectra.

Mass determination (m/z) takes place in the drift region of the TOF section by a precise time measurement of the drift time after acceleration of the ions in the orthogonal acceleration stage and their impact on the detector.

An electro-static field accelerates ions inside the source to a kinetic energy of several keV. After leaving the source (orthogonal acceleration stage) the ions pass a field-free drift region in which they are separated as a result of their m/z ratio. This separation is due to ions with a fixed kinetic energy and different m/z values being accelerated to different velocities in the ion source. The time of flight, in combination with values for the acceleration voltage and length of the drift region, allows for the determination of the m/z value of the ions.

2.3.6.4 Dual Stage Reflector

Due to the different velocities and positions of the ions prior to orthogonal acceleration, slight differences in final kinetic energy are observed. The primary task of a reflector is to normalize these energy differences and thus to improve resolution. Ions of the same mass but of unequal kinetic energies will penetrate the reflector field to different depths, which compensates for their varying starting energies.

The reflector in the maXis Series has two different stages. In the first reflection stage the incoming ions are decelerated from high velocities to relatively low flying speed. The second reflection stage softly slows the ions down to the reversal point and deflects them back to the flight tube. On re-entering the first reflection stage the ions get accelerated back to flight tube speed.

Accurate compensation for the varying starting energies is achieved as a result of the low flight speed in the second reflection stage.

To obtain high quality mass spectra with a reasonable signal-to-noise ratio the geometry of a reflector has to fulfill specific electrical and size requirements mainly with respect to the dimensions of the flight tube and type and size of the reflector, employed.

2.3.6.5 Detector

A detector converts an ion signal into an electrical signal. In the maXis Series the electrical signals from the TOF detector are transmitted to a digitizer card which is mounted in the PC.

2.4 External Connections

CAUTION

To avoid damage to the digitizer card, do **not** disconnect the signal lines before switching off the main power to both the mass spectrometer and the computer.

Figure 2-18 External Connections on the maXis Series

The following connections are accessible on the lower right hand side of the housing:

- Peripheral interface (HPLC system)
- Serial interface for the PC
- Digitizer input: For the patch cable of the signal adapter box
- Signal and trigger lines for the digitizer on the PC
- Main circuit breaker
- Switched socket inlet for the unit
- Switched socket outlet for the roughing pump (1200 VA)

- Collision gas inlet
- N_2 inlet 5.5 – 6 bar for the ion source (nebulizing and drying gas), and for venting the vacuum system

2.4.1 LED Display

The instrument is equipped with two groups of LEDs located on the lower right hand side at the front of the housing (see Figure 2-19).

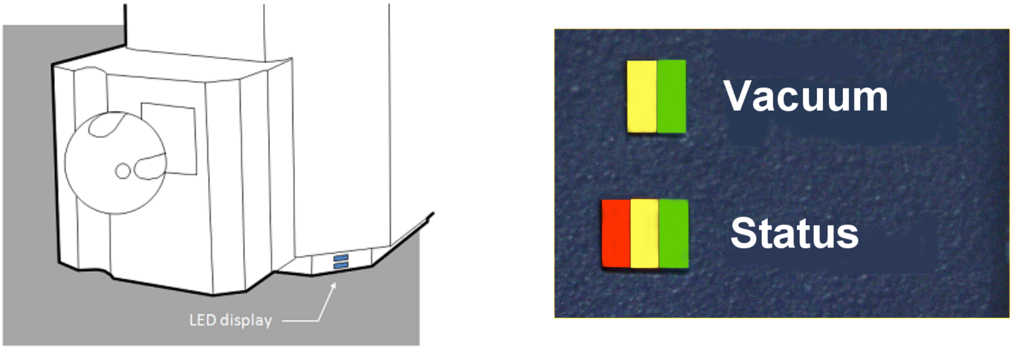

Figure 2-19 Left: Location of LEDs. Right: LED Display.

The table below explains what the LEDs mean, and how they display instrument status.

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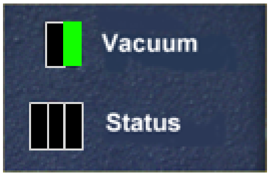
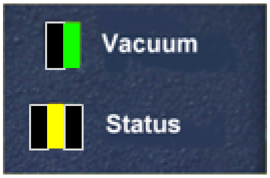
Shutdown
(green Vacuum LED)

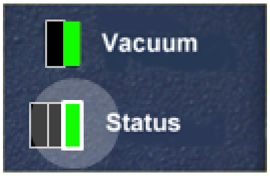


Standby
(green Vacuum LED + yellow Status LED)

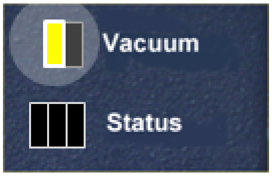


Operate
(green Vacuum LED + green Status LED)

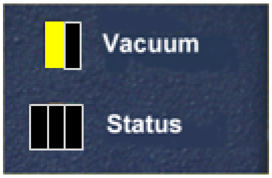
Aquisition
(green Vacuum LED + blinking green Status LED)



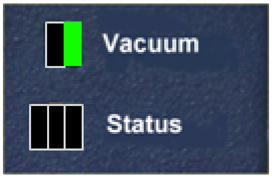
Venting
(blinking yellow Vacuum LED)



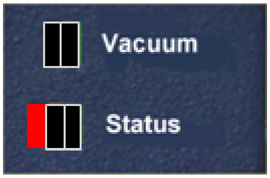
Vented
(yellow vacuum LED)



Pumping Down
(green Vacuum LED)



Error
(red Status LED)



2.4.2 Peripheral Interface (External start for data acquisition)

Table 2-1 Pin assignment of the peripheral interface

Pin	Signal	Remarks
1	Analog GND	
2 3	Analog Input 1 - Analog Input 1 +	differential inputs for Analog In 1; max. input voltage **10V**
14	Analog GND	
15 16	Analog Input 2 - Analog Input 2 +	differential inputs for Analog In 2; max. input voltage **10V**
7	Ready	digital output (open drain) must be connected with external pull up resistor to +5V (pin 12)
8	GND	
9	Stop	digital input to stop acquisition; is pulled up (10kΩ)
10	GND	
11	Start	digital input to start acquisition; is pulled up (10kΩ)
12	+ 5V	Voltage out
13	+ 24V	Voltage out

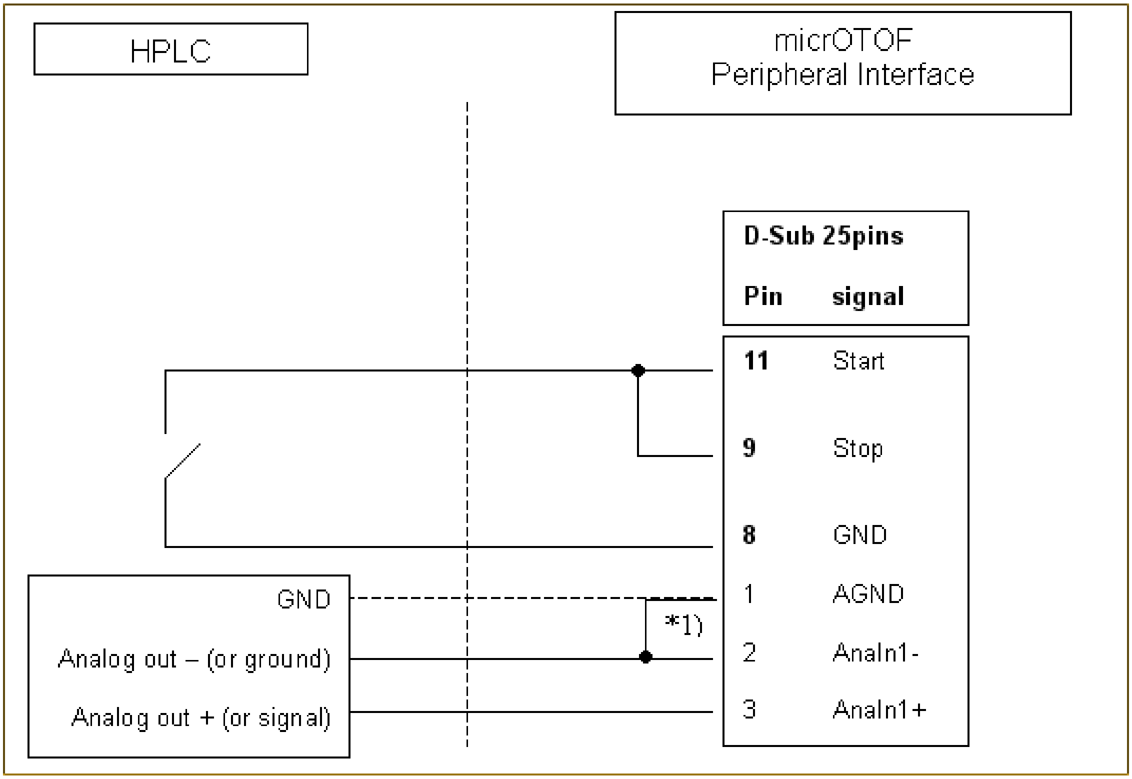


Figure 2-20 External Start / Stop acquisition function

*1) **Note:** Connection between AGND and AnaIn1- (Figure 2-20) should be made **only** when there is **no differential output** available on the HPLC.

Closed contact -> Starts acquisition.

Opened contact -> Stops acquisition.

Please refer to the corresponding **Software Settings** on the ***Mode*** page (Figure 2-21).

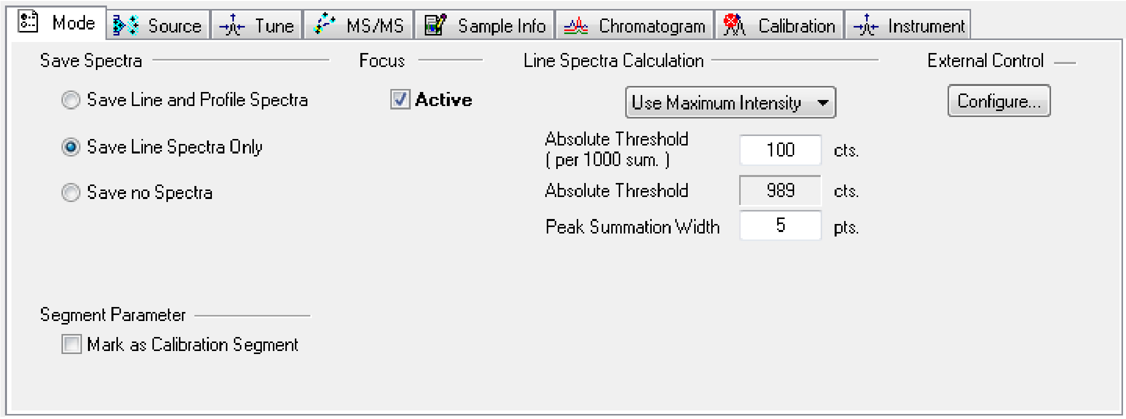


Figure 2-21 Features of the Mode page

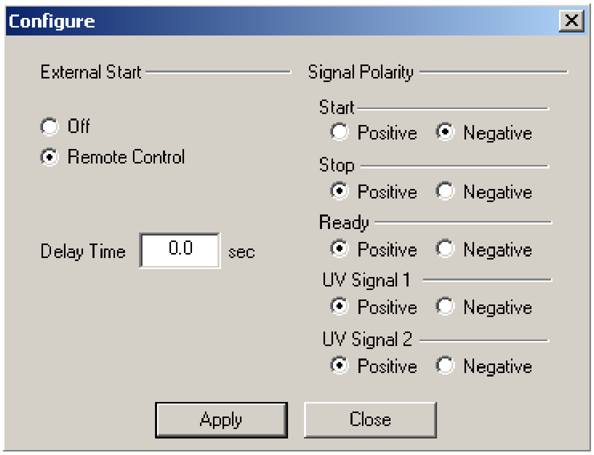


Figure 2-22 Configure dialog for external devices

2.5 PC Configuration

The PC controls the mass spectrometer, acquires and saves data to disk. The quad-core processor system makes rapid database queries possible.

On delivery, the system is likely to have the following configuration:

- Intel Quad-Core (IBM-compatible) processor
- RAM
- Hard disk
- DVD-ROM drive
- DVD±RW drive
- Digitizer PCI Express
- Graphics card
- Two LAN ports (Intranet, LC system)
- 24-inch color monitor, 1920 × 1080 resolution
- Microsoft® Windows® XP Pro (SP 3) or Microsoft® Windows® 7 operating systems.
- Control and application software (otofControl and DataAnalysis)
- Standard US Keyboard and Mouse
- Laser Printer b/w

Note Due to the variety of computer hardware, Bruker cannot support customer chosen computers for instrument control. If you need a new acquisition computer, please contact a Bruker representative in your area.

2.6 Remote Service

To maximize operating time, the instrument has a remote service capability (see Figure 2-23). This feature provides troubleshooting via the Internet with the customer PC being fully controlled by Bruker Service Hotline. Software and firmware updates can also be performed using this feature.

Note The otofControl PC must have Internet access to use the remote service capability.

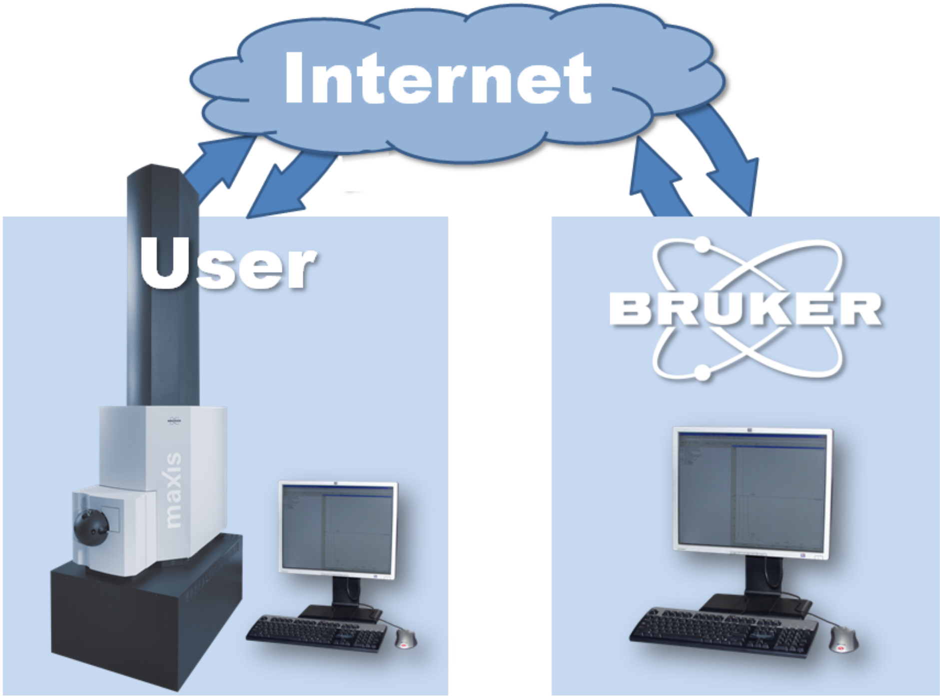


Figure 2-23 Operating principle of the remote service

2.6.1 Initiating Remote Service

►►To request a remote service session:

- Send an email to esitof.support@bdal.de providing the following information:
  - Your name and location.
  - The serial number of your instrument.

Bruker will contact you as soon as possible via email and provide instructions and a web link for a remote service session.

Note The connection between Bruker and the customer's PC is automatically severed when Internet Explorer is closed.

3 Understanding API- and APCI-Electrospray

This chapter provides an introduction to the processes that occur in API-electrospray and to the type of data that can be obtained.

3.1 Atmospheric Pressure Interface (API)

A liquid chromatograph / mass spectrometer (LC/MS) interface must perform three fundamental processes:

- Aerosol generation
- Ionization
- Solvent removal

In API-electrospray, the aerosol generation (nebulization) is a result of pressurized nebulizing gas combined with a strong electrical field. The strong electric field also aids in ionization. Solvent is stripped away by an inert warm gas. All three of these processes occur at atmospheric pressure, outside the vacuum region of the mass spectrometer, in a specially designed spray chamber.

The desolvated ions are directed into the low pressure region of the source through a sampling orifice - the capillary. Skimmers, an ion guide, and exit lens transport and focus the ions into a beam, while the nebulizing and drying gases are pumped away. The ions are thus transferred into the mass spectrometer for mass analysis.

This chapter is an introduction to the processes that occur in the ESI and APCI. For more information about ESI and APCI, refer to the list of journal articles at the end of this chapter.

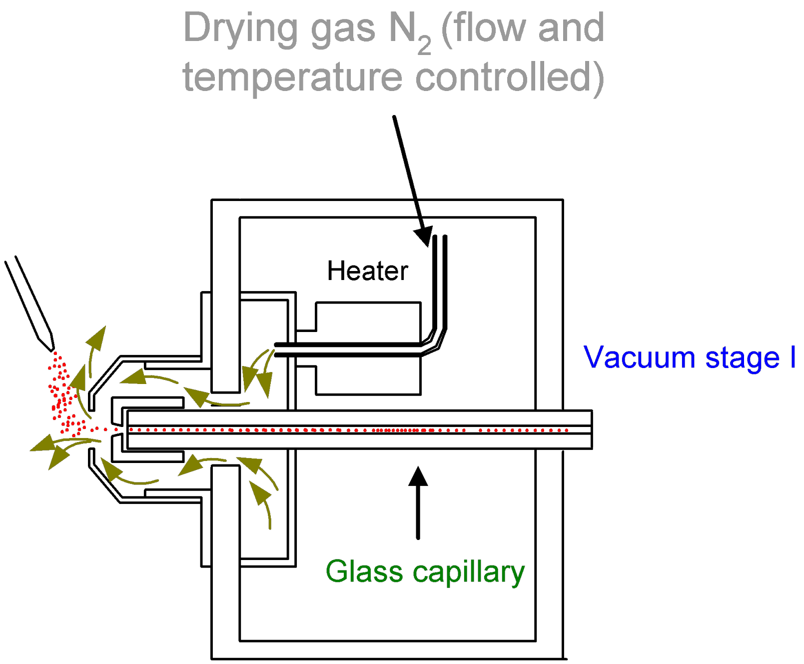


Figure 3-1 Electrospray ionization (flow of drying gas N2 and analyte)

3.2 How ESI works

The process of electrospray ionization (ESI) (API and APCI) can be summarized in four steps:

- Formation of ions
- Nebulization
- Desolvation
- Ion evaporation

Several different aspects concerning ESI have to be considered

- Importance of solution chemistry
- Positive ion analysis
- Negative ion analysis
- Formation of adduct ions
- Solvents
- Buffers

3.2.1 Process of Electrospray Ionization

The process of electrospray ionization (ESI) (API and APCI) can be summarized in four steps:

3.2.1.1 Formation of ions

Ion formation in API - electrospray occurs through more than one mechanism. If the chemistry of analyte, solvents, and buffers is correct, ions can be generated in solution before nebulization. When possible, and when done correctly, this results in high analyte ion abundance and good API - electrospray sensitivity.

Pre-formed ions are not a requirement for ESI. Analytes that do not ionize in solution can still be analyzed. The process of nebulization, desolvation, and ion evaporation creates a strong electrical charge on the surface of the spray droplets. This can induce ionization in analyte molecules at the surface of the droplets.

3.2.1.2 Nebulization

Nebulization (aerosol generation) begins when the sample solution enters the spray chamber through a grounded needle (see Figure 3-1). For high flow electrospray, nebulizing gas enters the spray chamber concentrically through a tube that surrounds the needle. The combination of strong shear forces generated by the nebulizing gas and the strong electrostatic field (2 kV to 6 kV) in the spray chamber draws out the sample solution and breaks it into droplets. As the droplets disperse, ions of one polarity are preferentially attracted to the droplet surface by the electrostatic field. As a result, the sample is simultaneously charged and dispersed into a fine spray of charged droplets - hence the name *electrospray*. Because the sample solution is not heated when the aerosol is created, ESI ionization does not thermally decompose most analytes.

The charged droplets contain analyte, solvent, and both positive and negative ions. The type of ions formed depends on the composition of the liquid sprayed. If, for example, the solution contains the sample in acetic acid with a positive potential on the needle, the predominant positive ions will be H_3O^+ and positively charged molecular analyte ions $[MHn]^+$.

3.2.1.3 Desolvation

Before the ions can be mass analyzed, solvent must be removed to yield a bare $[M+Hn]^+$ ion where n = 1, 2....

A counter flow of neutral, heated drying gas, typically nitrogen, evaporates the solvent, decreasing the droplet diameter and forcing the surface charges closer together (see Figure 3-2).

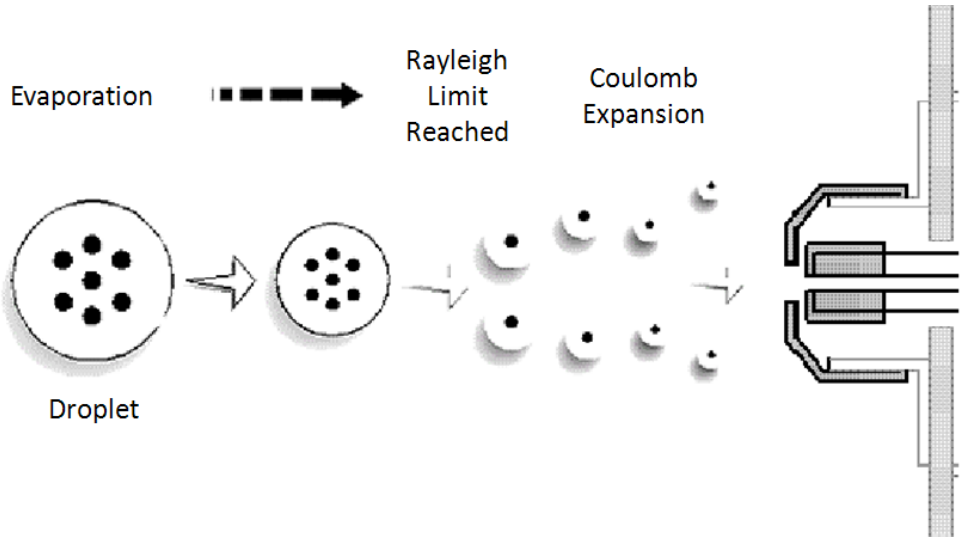


Figure 3-2 Coulomb explosions produce charged droplets within the spray chamber (• analyte)

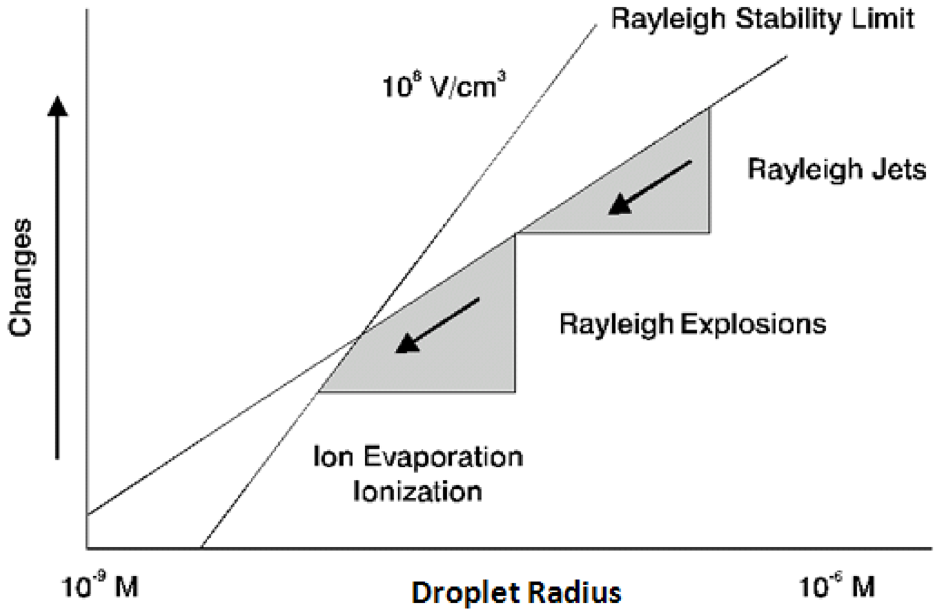


Figure 3-3 Process of ESI RAYLEIGH

When the force of the Coulomb repulsion equals that of the surface tension of the droplet (the Rayleigh limit – see Figure 3-3), the droplet explodes, producing charged daughter droplets that are subject to further evaporation. This process repeats itself, and droplets with a high surface-charge density are formed. When charge density reaches approximately 10^8 V/cm^3, ion evaporation will occur.

The choice of solvents and buffers is a key to successful ionization with electrospray. Solvents like methanol that have lower heat capacity, surface tension, and dielectric constant, promote nebulization and desolvation.

3.2.1.4 Ion evaporation

The process of ion formation has been the subject of many scientific investigations, yet different theories still exist regarding the specific physical process. The ion evaporation process described below is the model accepted by Fenn and others (6).

In the ion evaporation model (sometimes referred to as *ion desorption*), ions are emitted directly from the charged droplets into the gas phase. As solvent evaporates from the droplets in the presence of the strong electric field, the surface of the droplet becomes highly charged. When the field created by the ions at the surface of the droplet exceeds the surface tension, bare analyte ions are emitted directly from the droplet (Figure 3-4). This model was first described by Iribarne and Thomson (10).

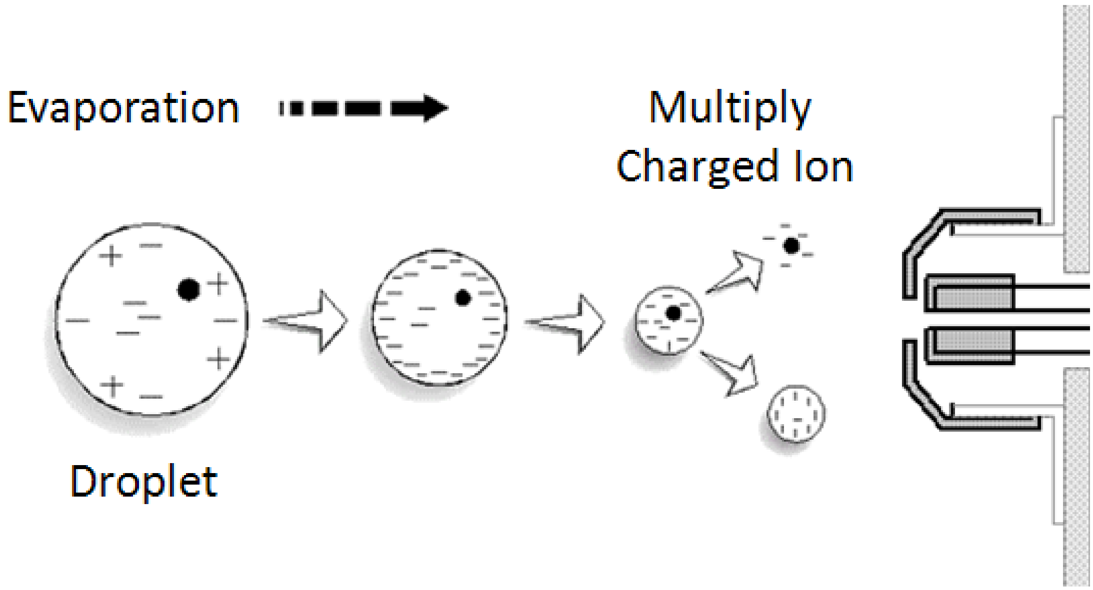


Figure 3-4 Ion evaporation mechanism within the ESI chamber (• analyte)

The hydration energy of the sample in a solvent dictates the ease of desorption of ions into the gas phase. In general, the more hydrophobic (less hydration) a sample is in a solvent (yet still soluble in that solvent), the better ions can be desorbed into the gas phase.

3.2.2 Different Aspects of ESI

Several different aspects of the ESI process should be considered:

3.2.2.1 Important Aspects of solution chemistry

Solution chemistry plays an important role in enhancing sensitivity for both positive and negative electrospray ionization. Many compounds can be analyzed as neutral molecules in a neutral environment. Other compounds, however, can be analyzed with much greater sensitivity if the chemical environment is one that favors ion formation.

When an analyte is dissolved in an acidic or basic polar solvent such as an acid or base, it can either ionize or take on a strong dipole moment. For analytes that ionize, ESI is generally simple and highly sensitive. Provided no other ion-ion interactions interfere, ions are already present in the solution before spraying. These ions are easily evaporated from the droplets in the spray and result in a high analyte ion abundance.

Analytes that form strong dipole moments but do not ionize can still be analyzed. The ionization process is driven by the strong electrostatic fields in the spray chamber. These fields induce a charge on the spray droplets. This charge can induce ionization in analyte molecules at the surface of the droplets. These analytes can also be ionized chemically by adduction using special chemicals.

3.2.2.2 Positive ion analysis

Analytes that are rather basic in character are generally analyzed in positive ion mode. The sample molecule (base) picks up a proton from the more acidic solvent solution.

$M^0 + HA \longleftrightarrow [M + H]^+ + A^-$

For very polar analytes, the process is in equilibrium. Ionization is enhanced by increasing the number of hydronium ions present. Solutions containing weak acids such as formic, acetic or propionic acid generally work best. Strong acids such as trifluoroacetic acid (TFA) and hydrochloric acid work poorly because the strong acid anion pairs with the analyte cations, reducing analyte ion abundance.

Analytes which have basic sites on the molecule, such as basic nitrogen functions, usually show high sensitivity in slightly acidic solutions (pH < 7). Those which have no basic nitrogen functions generally show a lower response in positive ion mode. Hydrocarbons have a very low response in positive ion mode.

3.2.2.3 Negative ion analysis

Analytes that are rather acidic are generally analyzed in negative ion mode. The sample molecule (acid) loses a proton and transfers it to a base (pH >7) in solution and becomes negatively charged. Therefore, for high sensitivity negative ion analysis, it is important to have a base in solution. Ammonia and other volatile bases yield best results.

For negative ionization, analytes with functional groups that deprotonate readily, such as carboxylic or sulfonic acids, show the best sensitivity. Analytes that are polar but contain no acid groups show less sensitivity.

Charge exchange is another mechanism that can occur in negative ion mode. It results in an $[M]^-$ ion instead of an $[M-H]^-$ ion.

In GC/MS electron capture often makes negative ionization the most sensitive operation mode. In ESI, electron capture is not a common ionization mechanism. Negative ionization is generally less sensitive than positive ionization in ESI.

It is also possible to switch from positive to negative polarity during a scan of a peak (Fast Polarity Switching) and to switch between positive and negative polarity in different segments of a scan.

3.2.2.4 Formation of adduct ions

Neutral molecules that do not readily dissociate, and do not protonate in the presence of the strong electric fields, can sometimes be ionized through adduct formation. Sugars can be adducted through the addition of a low concentration (50 micromolar) solution of an alkaline metal salt, such as sodium acetate or potassium acetate. Urea can be ionized in the same manner.

3.2.2.5 Solvents

ESI requires polar solvents. Non-polar solvents, however, can often be used successfully if a polar modifier is added. For example, toluene, a non-polar solvent, modified with 15% isopropyl alcohol can be used as a solvent for the ESI analysis of fullerenes in negative ion mode. The following table includes examples of other solvents that can be used for normal-phase chromatography when modifiers are added.

For positive ionization, mixtures of acetonitrile/water, methanol/water, and isopropyl alcohol/water are most common but other mixtures can be used with success. Acetonitrile/water, isopropyl alcohol/water and n- propyl alcohol/water are good starting mixtures for negative ionization.

API- electrospray sensitivity is best with either acetonitrile or methanol and water. Typically, the pH of the mobile phase is adjusted in order to cause the highest yield of ionization in the solution phase.

Partial list of solvents and their suitability for ESI

Commonly used	Special cases
Water (<80%)	Benzene[1]
Methanol	Carbon disulfide[1]
Ethanol	Carbon tetrachloride
n-Propyl alcohol	Cyclohexane[1,2]
Isopropyl alcohol	Hexane[1]
t-Butyl alcohol	Ligroin[1]
Acetonitrile	Methylene chloride[1,2]
Acetone	Toluene[1,2]
Tetrahydrofuran	
Acetic acid	
Formic acid	
Chloroform	
Formamide	

[1]*Requires modifier.*
[2]*Normal-phase chromatography.*

3.2.2.6 Buffers

Buffers are used for many reasons including:

- Adjusting solution pH to support ion formation in solution (generally, positive analyte ions are formed more readily in acidic solutions and negative analyte ions are formed more readily in basic solutions)
- Ensure formation of specific desired adduct ions or prevent the formation of undesirable adducts
- Assist or optimize chromatography

If you are using chromatographic separation, some consideration must be given to why a buffer is added. Buffers that assist or optimize chromatography and those that do not hinder the electrospray process can be added before the separation. Buffers that interfere with the separation must be added post column.

For most positive ion analysis of polar materials such as amino acids, peptides and proteins, the pH of the solution should be adjusted to a pH of 2 – 5. The addition of acetic acid at 0.1% to 0.2% is a good starting point. For positive ion analysis of pharmaceuticals, a solution of 0.015 % formic acid serves the same purpose and may have less chemical noise and smell than acetic acid. Some pharmaceutical compounds can be analyzed successfully in a neutral mobile phase. For example, benzodiazepines and opiates can be analyzed with a traditional mobile phase of acetonitrile and water.

Buffers such as sodium acetate or potassium acetate (alkali metals) can be used to form adducts with the analytes that would otherwise not ionize in solution. Sugars and urea are two examples of chemicals that form sodium adducts that can be analyzed in positive ion mode. Other buffers, such as ammonium acetate and ammonium formate, are sometimes added to prevent undesired adduction of the analyte with sodium or potassium ions from endogenous sources.

Buffers can be used to optimize chromatography. The addition of 50 micromolar ammonium acetate or ammonium formate is often used to increase chromatographic resolution of basic nitrogen containing compounds on reversed-phase silica columns. This improves the peak shape, thereby enhancing signal and improving sensitivity. The final solution (solvent + analyte) should be neutral to acidic for good positive ionization.

Buffers or other additives used to optimize chromatography can sometimes interfere with the ionization process. For example, TFA is almost always used for the chromatography of peptides and proteins. TFA enhances the chromatographic resolution but may actually suppress ion formation. Post-separation addition of a weaker acid such as propionic acid can effectively counteract the TFA ion suppression problem (23).

When performing ESI standard buffers such as phosphate, borate, and sulfate buffers are non-volatile and form ion pairs in solution. To maximize ESI sensitivity, use buffers that are volatile and do not form ion pairs. Adjust the pH with buffers, formic acid, acetic acid, and ammonium hydroxide or triethylamine. Typical pH for positive ion is neutral to pH 2 and for negative mode typical pH is neutral to pH 10. For ion pair separations, use additives such as heptafluoro butyric acid or tetraethylammonium hydroxide or tetrabutylammonium hydroxide.

3.3 How APCI works

What is the difference between ESI and APCI?

APCI is a gas phase chemical ionization mechanism very similar to methane or ammonia CI in GC/MS. In APCI the CI reagent gas is the HPLC mobile phase: such as water, methanol or isopropanol. The vaporized mobile phase (reagent gas) reacts with electrons from the corona discharge to form various adduct ions. These adducts, based on proton affinity, will transfer a proton, in the case of the positive ion mode, to the analyte. Depending on the analyte and solvent system, other reactions are possible:

- Protonation (such as H_3O^+ and bases)
- Charge exchange
- De-protonation (acids)
- Electron capture (halogens, aromatics)

APCI requires that the analyte must be in the gas phase to occur for ionization. To bring the mobile phase and analyte into the gas phase APCI is typically operated at vaporizer temperatures of 400 °C – 500 °C.

In APCI, the vaporizer temperature must be carefully controlled. Most compounds work best at higher temperatures while a few compounds work best at lower temperatures. It may be necessary to evaluate a couple of temperatures to determine the optimal APCI vaporizer temperature.

3.3.1 When to Use APCI

There are some reasons – and also some requirements - that will require a change to APCI to get better results:

- Sample exhibits a poor electrospray response
- Sample contains no acidic or basic sites
  (such as hydrocarbons, alcohols, aldehydes, ketones, esters)
- Sample is thermally stable and can be vaporized
- Flow rates, solvents or additives are not compatible with electrospray
- Ease of operation (such as eliminating a post-column Tee)

3.3.2 APCI Solvents

Mobile phases for APCI LC/MS is preferably an aqueous-organic solvent combination with 2 mMol – 20 mMol of volatile organic buffer. The following solvents are typical APCI mobile phase solvents and buffers. High concentrations of acetonitrile (ACN) should be avoided and its use has been shown to quickly carbonize the corona needle which can lead to reduced total ion current.

Common Solvents	Common Buffers
Methanol	Acetic Acid
Propanol	Formic Acid
Butanol	Heptafluoro Butyric Acid
Acetonitrile	Ammonium Acetate
Acetone	Ammonium Formate and Acetate
CH_2Cl_2	Ammonium Hydroxide
Toluene	Triethylamine
Ethanol	Tetraethylammonium Hydroxide
Isopropanol	Tetrabutylammonium Hydroxide
Water	
CCl_4	
Benzene	
Hydrocarbons (such as Hexane, Cyclohexane)	

When performing APCI standard buffers such as phosphate, borate, and sulfate buffers are non-volatile and form ion pairs in solution. To maximize APCI sensitivity, use buffers that are volatile and do not form ion pairs. Adjust the pH with buffers, formic acid, acetic acid, and ammonium hydroxide or triethylamine. Typical pH for positive ion is neutral to pH 2 and for negative mode typical pH is neutral to pH 10. For ion pair separations, use additives such as Heptafluoro butyric acid or tetraethylammonium hydroxide or tetrabutylammonium.

3.3.3 Achieving Gas Phase Conditions

In APCI, the probe temperature is the most important parameter to achieve good sensitivity and minimal decomposition. Many compounds do ionize at high vaporizer temperatures. For example, compare the response of Vitamin D3 (compound 7) and Furosemide (compound 9) where the vaporizer temperature was lowered from 400 °C to 200 °C.

At 400 °C, significant response for these compounds was observed (Figure 3-5).

At 200 °C, low response for these compounds was observed (Figure 3-6).

Table 3-1 Detected Compounds in Figure 3-5 and Figure 3-6

1	Penicillin G	9	Furosemide
2	Cloxacillin	10	Spectinomycin
3	Tetracycline	11	Gentamicin
4	Sulfamethazine	12	Streptonycin
5	Sulfamethizole	13	Disperse Orange 13
6	Amino Chlorobenzamide	14	Basic Yellow 2
7	Vitamin D3	15	Basic Violet 10
8	Methylene Blue	16	Disperse Blue 3

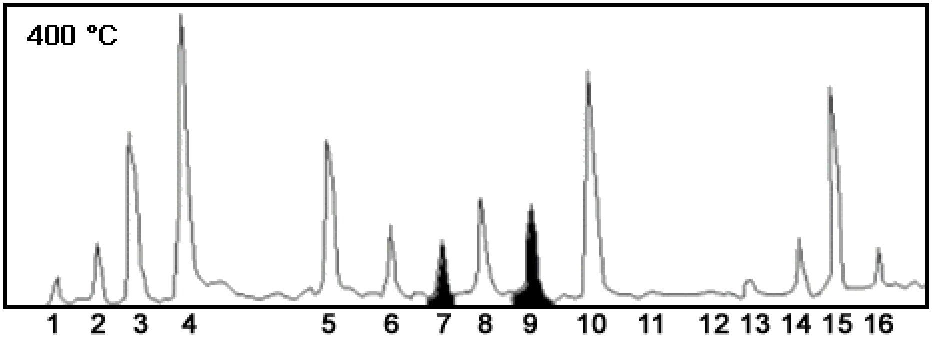


Figure 3-5 Vaporizer temperature at 400 °C with significant response of compound 7 and compound 9

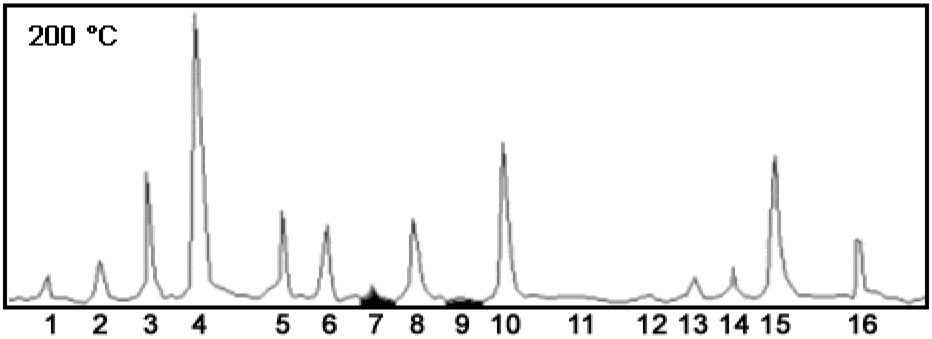


Figure 3-6 **Vaporizer temperature at 200 °C with low response of compound 7 and compound 9**

3.4 Reference articles

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3.4.1 Reference articles for ESI

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4 Understanding maXis Series - Basic Principles

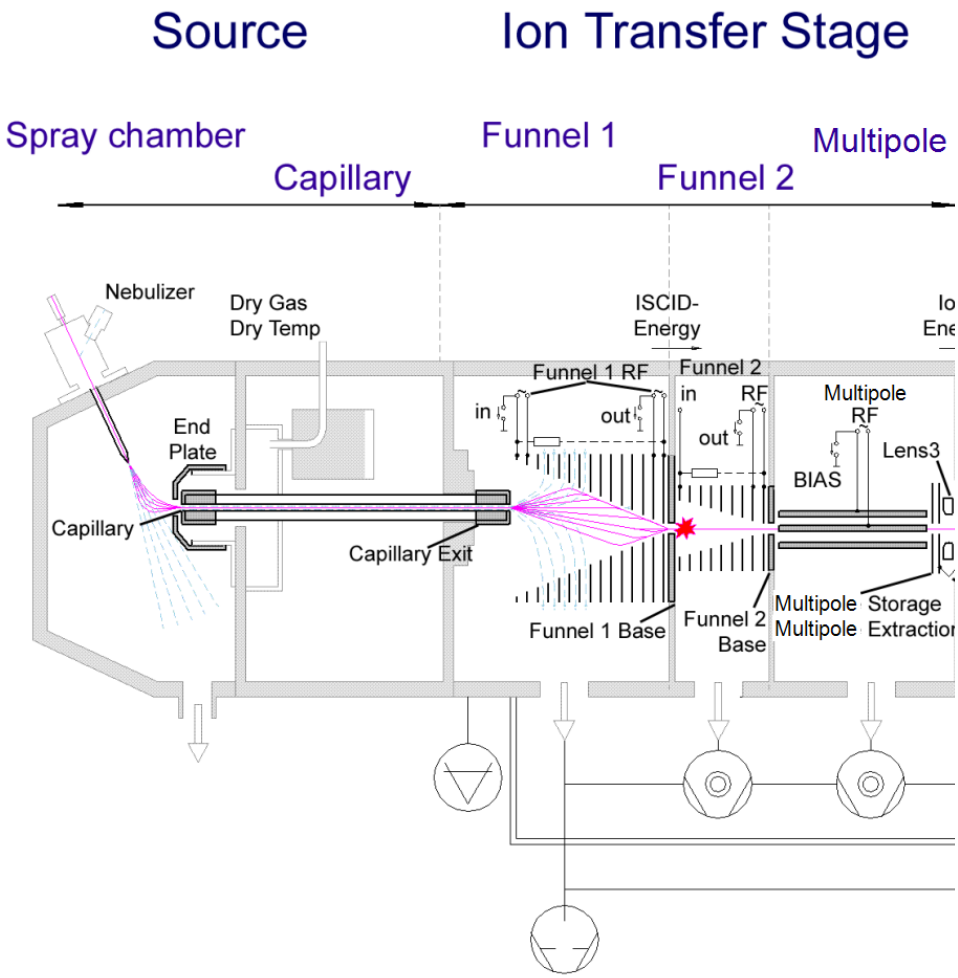


Figure 4-1 **Route of the ions through the maXis Series**

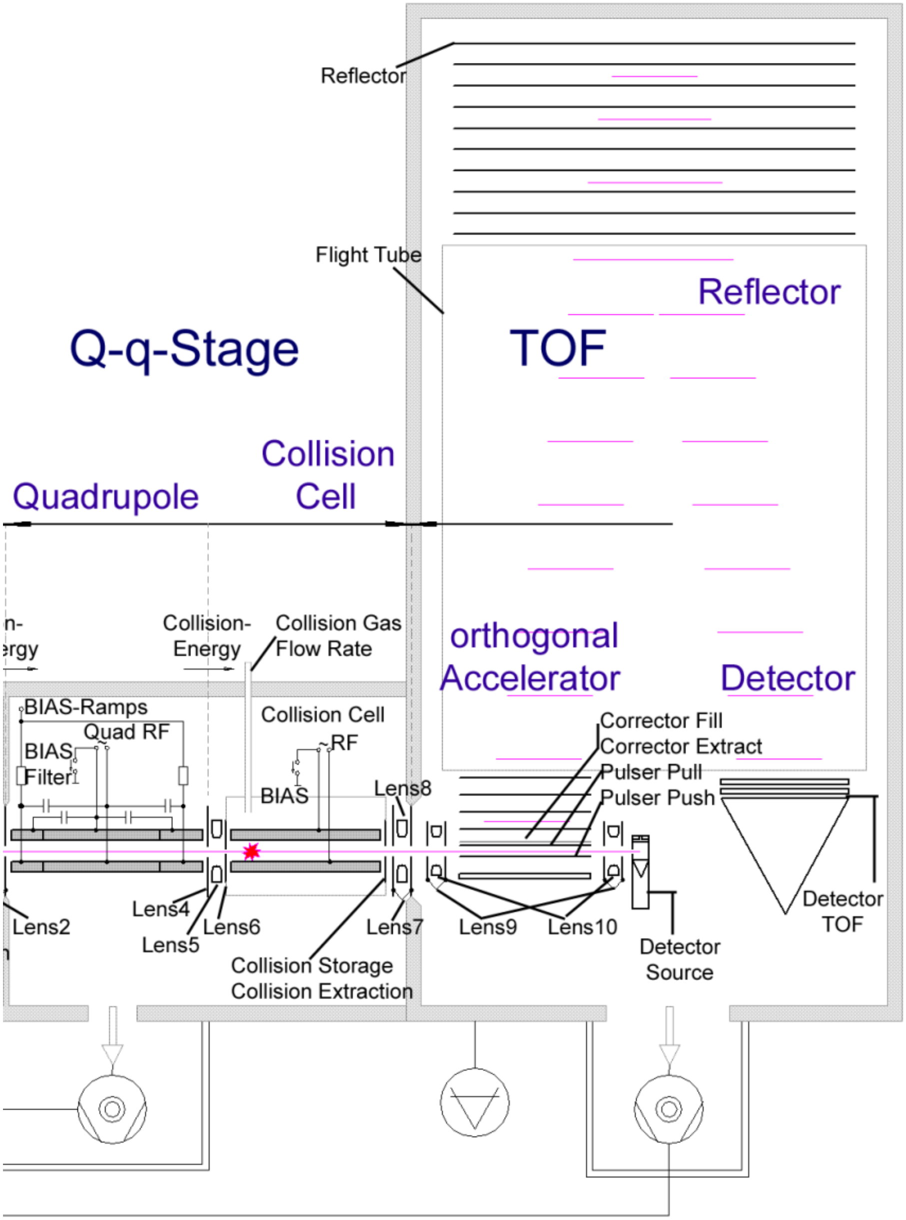


Figure 4-2 **maXis Series schematic showing the path of the ions through the Quadrupole, Collision / Cooling Cell and the TOF Spectrometer**

4.1 maXis Series as an API - MS/MS Instrument

In API techniques like ESI and APCI, ions are formed at atmospheric pressure. However, mass analysis of individual molecules can only be performed in high vacuum. Hence, the ions are to be introduced into the mass analyzer, passing several pressure stages. The ion guides in the transfer system allow for an efficient ion transfer to the analyzer while the neutral gas molecules are removed by the pumping system.

MS/MS is an indirect method of obtaining structural information. Characteristic compounds are isolated by the first MS stage since it is almost impossible to get direct information on the structure of complex, but low abundance, molecules. This isolation is performed in the mass resolving Quadrupole Mass Spectrometer which only transmits a narrow mass range when it is operated in mass selective mode.

In order to obtain structural information on this isolated compound it is forced to react. In the maXis Series the isolated ions are injected into the collision cell which serves as reaction chamber. The kinetic energy of the injected ions is at least partially converted into internal energy of the ions, giving rise to fragmentation if this internal excitation exceeds the dissociation energy of the molecular ions. The fragmentation induced by gas collisions is known as collision induced dissociation (CID).

The reaction products, i.e. the fragments, are analyzed in the second MS stage. Therefore the ions are extracted from the collision cell and injected into the TOF analyzer. The fragment spectrum gives structural information, as well as some energetic information, on the isolated molecules from the sample.

In MS mode, the quadrupole is used as an ion guide (RF only mode), not isolating an arbitrary mass, but transmitting a broad mass range. The collision energy is set very low in order to keep the internal excitation low and to avoid fragmentation.

4.2 Ion Guides

The maXis Series uses several types of ion guides. Funnels and multipoles are used to guide ions from the capillary exit to the analyzer, passing through several vacuum stages. An ion guide acts like a tube for charged particles, keeping the ions together but allowing the neutral gas and solvent molecules to escape from the ion path. Hence, the ions are brought into the analyzer with high transmission efficiency, but the neutral molecules are removed from the system by the pumping system.

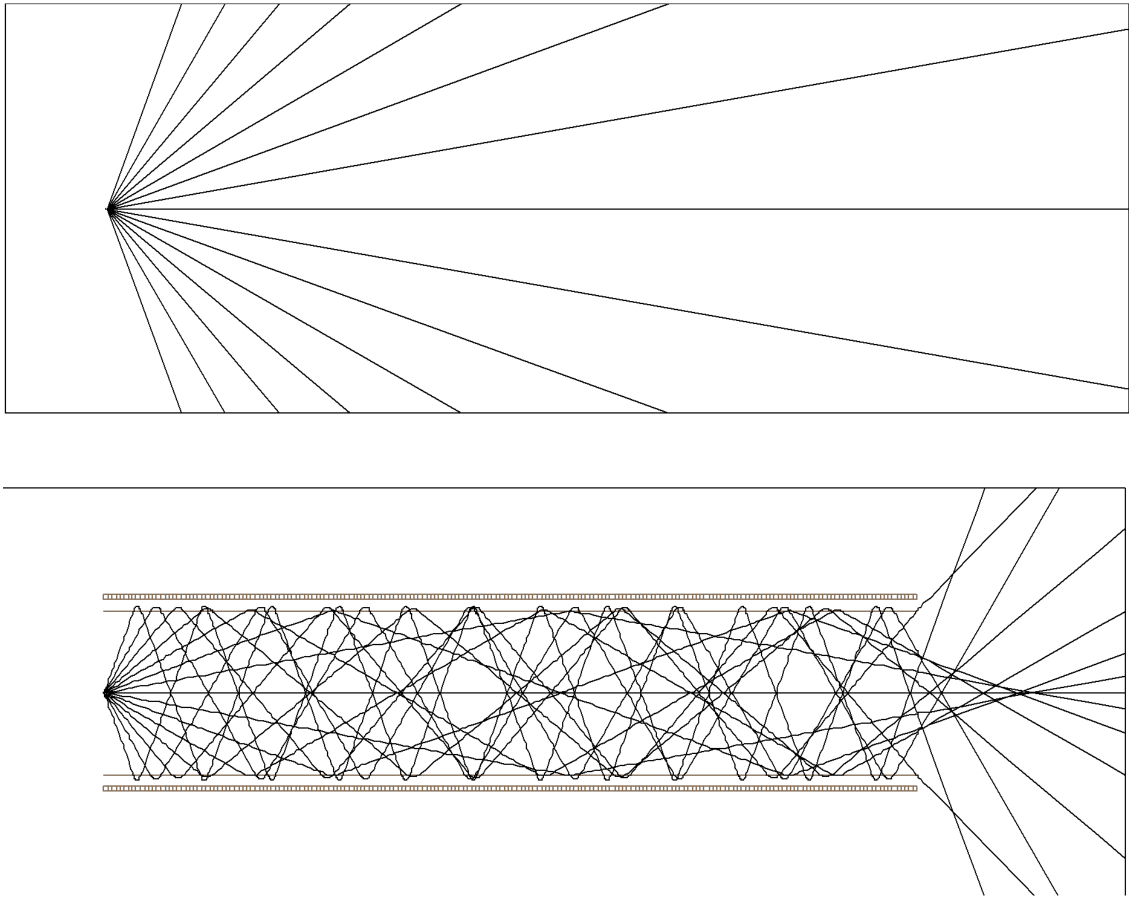


Figure 4-3 Ion Guide (principle): The ions cannot escape from the ion guide. Hence, they are guided over a distance with high efficiency.

The repulsive force in the ion guide keeping the ions focused on the center line arises from the interaction of the ions with the inhomogeneous RF field. Due to the inhomogeneity of the RF field (visualized by the electric flux lines) the initial motion of the ions towards the ion guide couples with the RF oscillation. The ion is pushed up and down (or back and forth) tangentially to the flux lines of the oscillating electric field. Due to the curvature of the flux lines, there is always a component of the force pushing the ions towards the weaker field. Hence, an ion moving towards the electric field will be decelerated and - if the repulsive force of the RF field is strong enough - reflected.

This behavior of ions in an inhomogeneous RF field is described as the Effective Potential or Pseudopotential or as the Ponderomotive Force. The effective Potential can be calculated by $V^* = e \cdot E_0^2/(4m\omega^2)$ and is a function of the local field strength, the ion mass (and charge) and the RF frequency.

The initial energy of the ion is transferred into RF oscillation and back into translational motion. Thus, the motion of the ion acts like a potential barrier. The ion energy in the pseudopotential equals the mean kinetic energy in the RF oscillation.

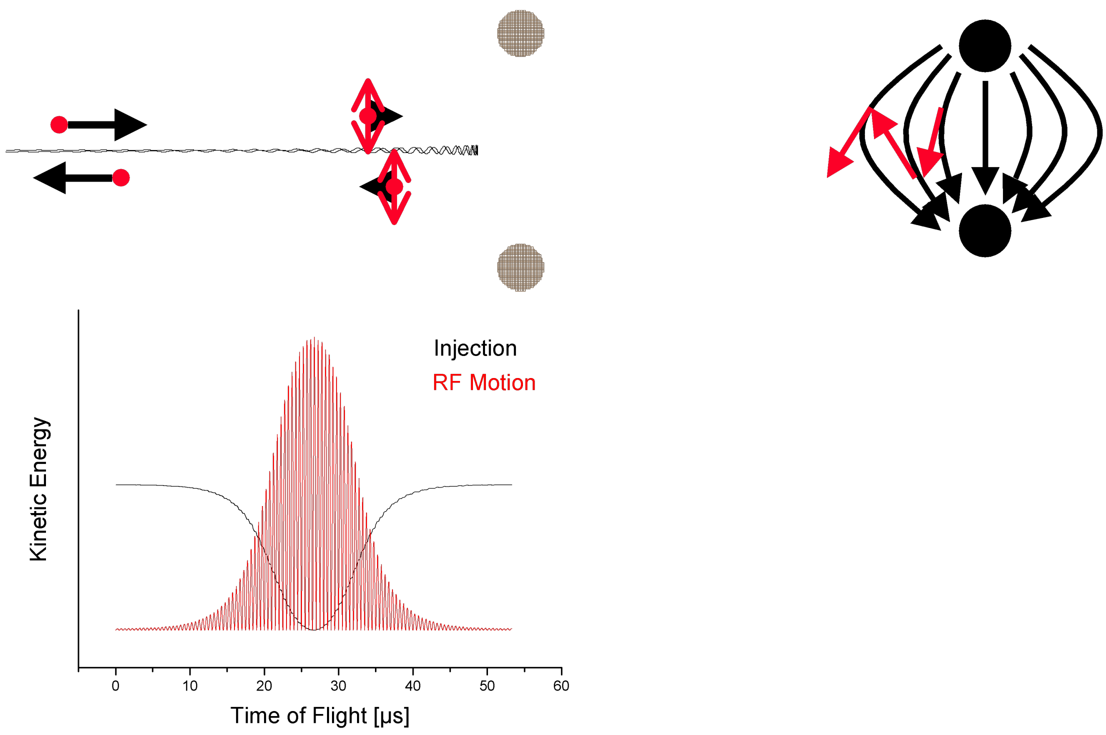


Figure 4-4 **The translational energy of the ion is converted into RF oscillation and back into translational motion. Thus, the motion of the ion in the RF field acts like a potential barrier, reflecting the ion. The ion energy in the pseudopotential equals the mean kinetic energy in the RF oscillation**

4.3 RF Ion Guides: closed repulsive wall

The inhomogeneous field can be extended by adding further electrodes forming a repulsive line, or, if we consider rod electrodes, a repulsive wall. This “wall” may be converted into a “tube” by wrapping it around an axis parallel to the rods, ending up with a multipole with 4 (quadrupole), 6 (hexapole) or more rods.

The repulsive “wall” might also be wrapped around an axis perpendicular to the electrodes, ending up with a stack of rings. A variant of this Stacked Ring Ion Guide is the Ion Funnel in which the ring electrodes have different diameters. An Ion Funnel efficiently collects ions exiting from the capillary and focuses them onto an orifice leading to the next vacuum stage. Furthermore the ions can be pushed gently towards the funnel exit by an axial DC gradient.

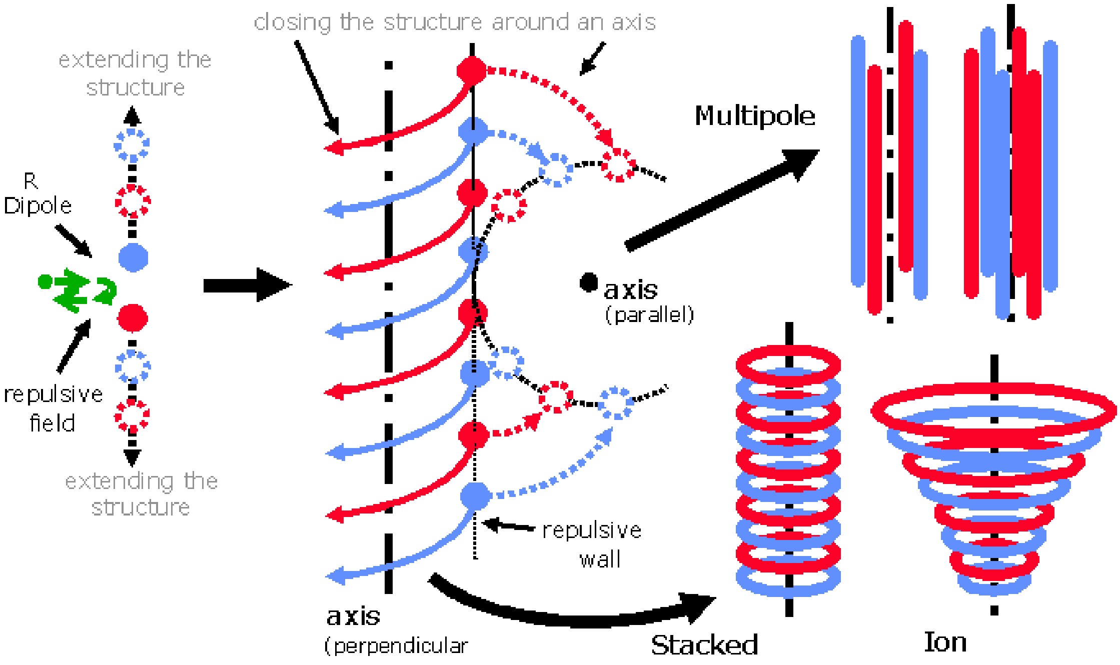


Figure 4-5 Getting the structure for the funnels from theory

4.4 Quadrupole Mass Spectrometer (Q-MS)

As discussed in chapter 4.2 a multipolar RF field creates a potential well for charged particles. In a quadrupole this field is quadratic, allowing for **harmonic** oscillations. This means, the oscillation frequency depends **not** on oscillation amplitude, but only on mass, RF frequency, RF amplitude and field dimensions. An RF-only quadrupole is suitable as an ion guide. The (RF) effective potential is always repulsive, pushing the ions towards the ions guide axis.

However, the pseudopotential V* acts on q/m and thus depends also on mass.

Applying a DC voltage to the opposite rod sets also creates quadratic potential, but this potential is only focusing (repulsive) (+U) in one dimension, while it is attractive (defocusing) (-U) in the other dimension perpendicular to the axis. The static potential acts only on the ion’s charge q.

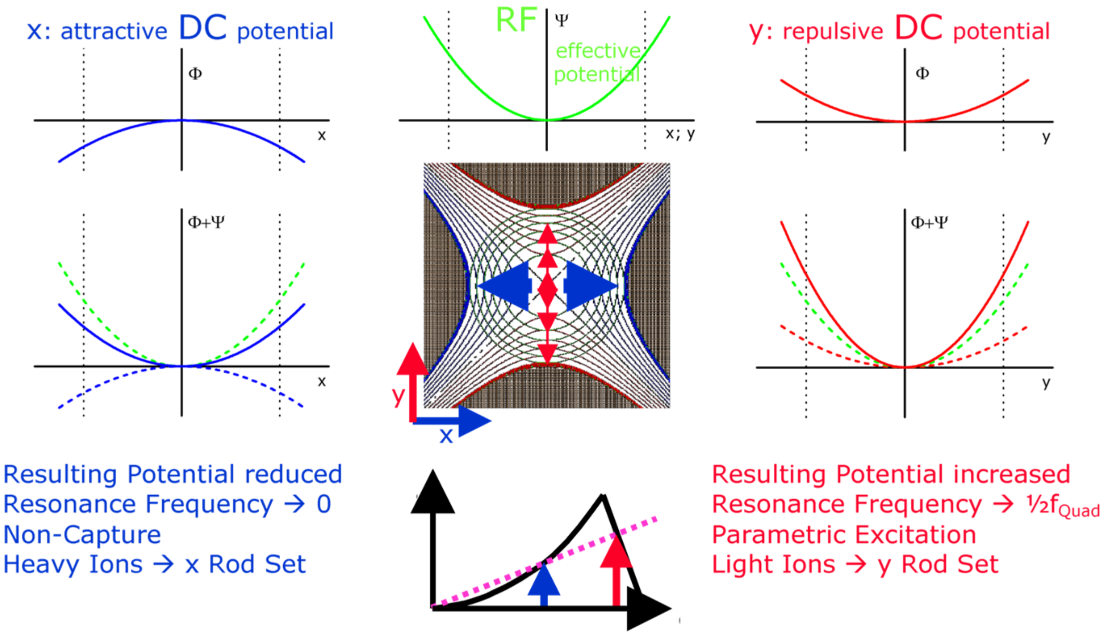


Figure 4-6 Resulting (pseudo)potential

Consequently, the resulting potential is also quadratic, if an RF and a DC potential are applied to the quadrupole at the same time.

In one dimension the RF pseudopotential (V*) and the DC (-U) act against each other. The resulting potential V*-U may also become negative.

As long as the effect of the pseudopotential dominates over the attractive DC potential, the ions will still pass through the quadrupole. If the static potential overcomes the pseudopotential, the ions will hit the rods with the attractive DC potential. Since the pseudopotential decreases with increasing mass, the heavier ions will be lost first. Figure 4-7 shows this on the left side. Since the resulting potential has also to overcome the thermal energy of the particle, the transmission fades away very softly for the heavy masses.

In the other dimension both potentials are repulsive. Hence, the effects of the pseudopotential and the DC potential support each other. The resulting potential V*+U provides a well for the fundamental oscillation of the ions. Since the resulting potential is higher than V*, the resulting fundamental frequency is also increased.

On the other hand, ions may couple with the quadrupolar RF field by parametric resonance. Ions will exchange energy with the RF field if the fundamental frequency meets half the quadrupole operation frequency.

Considering a full fundamental oscillation cycle and assuming the ion starts on the left side, the ion follows the pseudopotential, moving to the axis. During this first quarter of the fundamental oscillation, the ion also gets energy from the RF field. After the ion crossed the axis (i.e. in the second quarter of the fundamental cycle), the RF phase changes its polarity, causing the ion to lose less kinetic energy then it obtained during the first quarter. In the third quarter of the fundamental oscillation (ion moves back to the axis) the RF phase has changed its polarity again. Hence, the ion converts its energy from the pseudopotential plus some extra energy from the RF into kinetic energy. In the fourth quarter (ion moves from the axis to the left side), the RF phase is reversed again, causing the ion to lose less energy then it gained earlier.

This is very similar to a swing: From each reversal point of the oscillation to the lowest point one lowers the center of mass, getting some extra energy from the gravitation field, while one lifts the center of mass on the way from the lowest point to the highest point.

The up-and-down movement of the center of mass is the parametric excitation, whilst the oscillation of the swing is the fundamental oscillation.

Due to the resonant excitation, the transmission of lighter ions falls rapidly if there is parametric resonance.

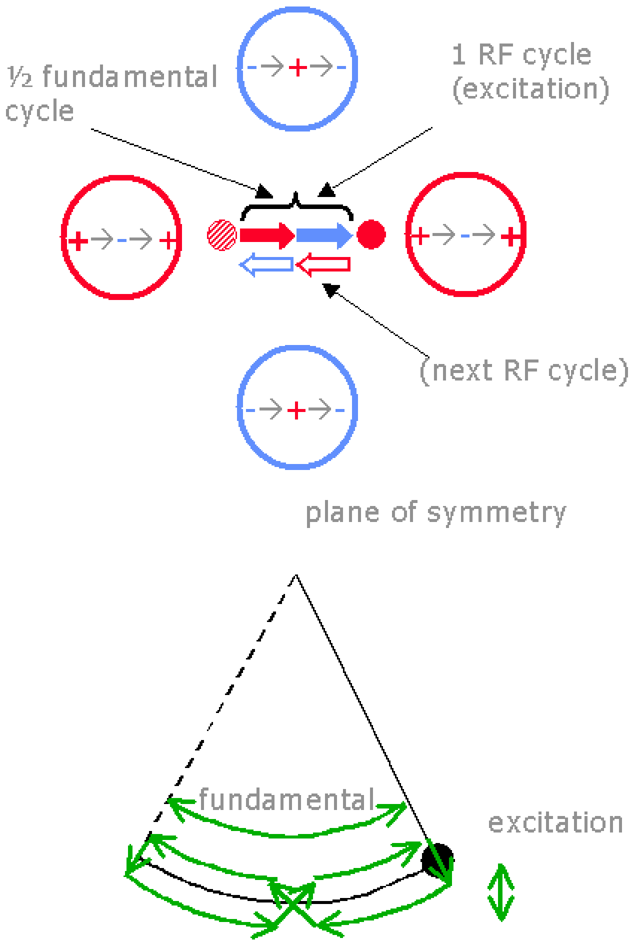


Figure 4-7 **Plane of symmetry**

This behavior is also reflected in the stability diagram for the quadrupole. The triangle is an excerpt from the diagram of the stability regions of the Matthieu differential equation.

The q-axis represents the RF, whereas the a-axis represents the DC. (The q-axis itself represents the RF-only quadrupole which can be used as an ion guide). Only ions within the nearly triangular shaped area are transmitted by the quadrupole. For them there are stable trajectories.

Adding a DC always narrows the transmission mass range of the quadrupole.

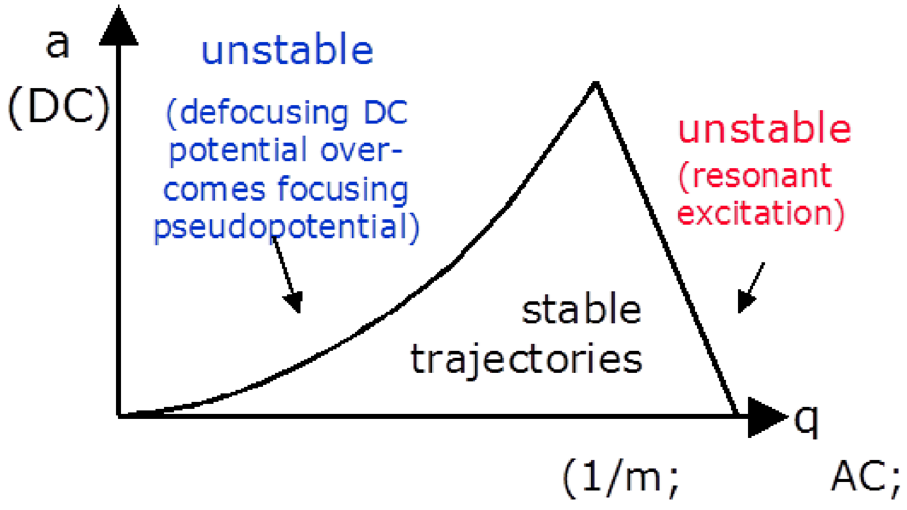


Figure 4-8 Stability diagram

On the left hand side of the triangle, the heavy ions are lost because the DC pushes them towards the rods.

On the right hand side the ions couple with the RF field. Due to the resonant excitation, this edge is sharp, and it is nearly linear because the resulting field grows linearly with the DC voltage applied to the quadrupole.

The mass selective quadrupole in the maXis Series is located between two short segments of RF-only quadrupoles. These segments significantly improve the acceptance behavior and the transmission efficiency of the mass selective quadrupole because the resolving DC heavily distorts the beam profile.

The operation of a mass selective quadrupole can by summarized as follows:

1. The effective potential (RF) focuses the ions.
2. The DC potential focuses one dimension, but defocuses the other dimension.
3. Heavy ions will hit the attractive rods due to the dominant DC attraction.
4. Light ions will hit the repulsive rods due to parametric excitation.
5. Ions are transmitted if the RF is dominant, but does not excite fundamental oscillation.
6. Quadrupolar field is two dimensional. Hence, injection and ejection are to be considered.

4.5 Collision Cell

The collision cell provides a reaction chamber for indirect structural analysis. The ions isolated in the quadrupole are injected with some arbitrary energy into the collision cell. The molecular ions collide with the gas atoms (or molecules, if N_2 serves as collision gas). Due to the gas collisions, translational energy of the ions is converted into internal (vibrational) excitation. If the internal energy overcomes the dissociation energy, the ion may dissociate into fragments.

In general, a complex ion may dissociate in different reaction channels, requiring appropriate dissociation energies. The injection energy, and thus the internal excitation, can be chosen arbitrarily allowing also for higher energetic dissociation channels. Hence, the fragment spectrum is not only a function of molecular structure, but it is also a function of internal energy and thus, of injection energy (and the collision gas).

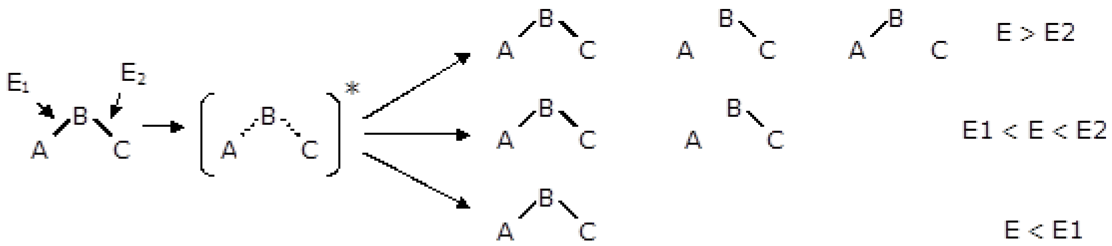


Figure 4-9 Fragmentation: Structure and Energetics

The conversion of translational energy into internal energy is correlated with momentum transfer. The amount of translational energy to be converted into internal excitation of the molecules is not only a function of the kinetic energy itself (and thus, of the injection voltage and the ion's charge), but it is also a function of the ion's mass as well as the collision partner's mass. The conversion efficiency increases with the collision gas molecular mass m' and can be estimated as $\Delta E/E = (4m')/m$.

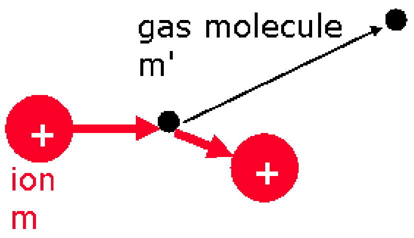


Figure 4-10 **Energy Transfer / Momentum Transfer**

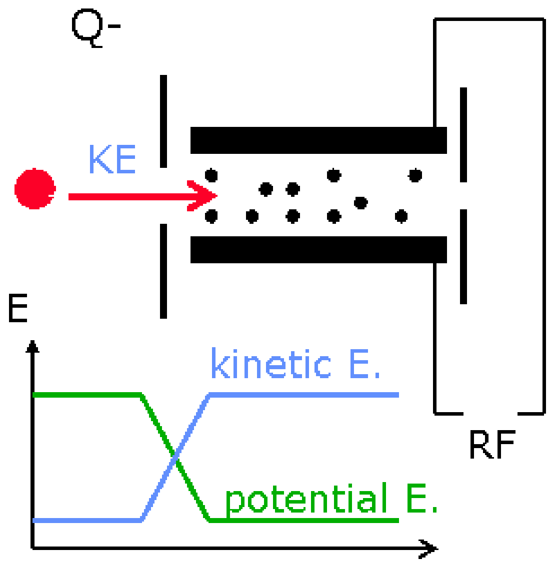


Figure 4-11 **Collisional Excitation**

The hexapole in the collision cell acts as an ion guide or two-dimensional ion trap, keeping the mother ions as well as the fragment ions together and close to the multipole axis. Thus, the ions are extracted very efficiently and injected into the cooling cell.

maXis HD, maXis plus and maXis instruments being upgraded with the HDC-cell have a quadrupolar collision cell. The total length of the HDC-cell is twice as long as the hexapolar collision cell and therefore collisonal cooling inside the HDC-cell is highly efficient. The HDC cell ends with a gate lens and a transfer lens and is directly coupled to the orthogonal TOF assembly.

4.6 Cooling Cell

The cooling cell is an additional pressure stage which further reduces pressure in the orthogonal acceleration stage and extends the cooling and focusing range. Due to the influx from the collision cell there is still a reasonable amount of collision gas molecules inside the cooling cell. Without applying additional collision energy, analyte ions continue to collide with collision gas molecules but the energies are too low to induce fragmentation. Instead the multiple low energy impacts reduce the translational energy of the ions, they get “cooled” down, and hence are well focused along the multipole axis before entering the orthogonal acceleration stage.

4.7 TOF Assembly

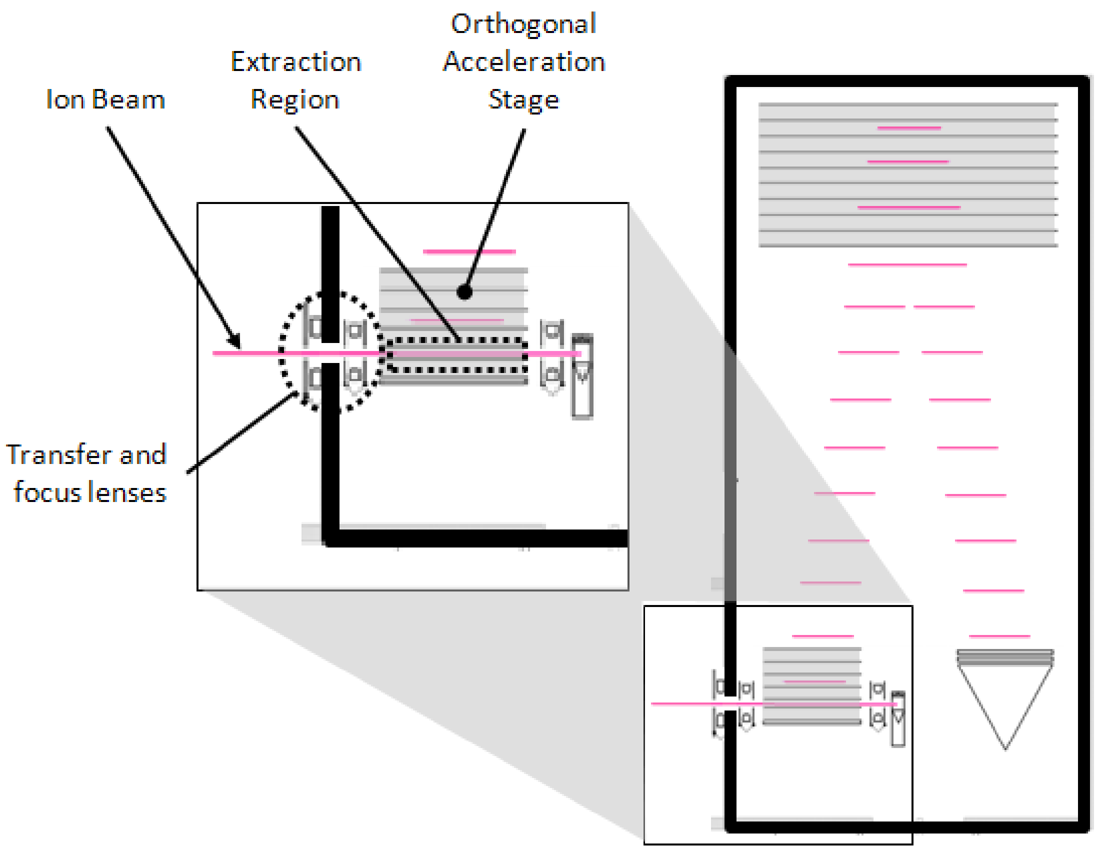


Figure 4-12 Schematic of the TOF assembly

The layout of the TOF assembly is shown in Figure 2-15. The main components of the TOF assembly are:

• Orthogonal acceleration stage (see section 2.3.6.1)).

• Reflector (see section 2.3.6.4).

• Detector (see section 2.3.6.5).

In ESI-TOF applications the orthogonal acceleration stage replaces the ion source. This stage does not create ions, but simply deflects and transfers incoming ions to the reflector by the use of pulsed voltages.

During pulser off time, when electrodes of the acceleration stage are maintained at ground potential, the incoming ion beam is guided directly to the conversion dynode of the SEM (Secondary Electron Multiplier) (Figure 2 15Figure 2 15). This set-up is used for monitoring ions, and can be used for troubleshooting or tuning the ESI-System. This detector is not used to acquire spectra!

4.7.1 Orthogonal TOF: Injection

The lens system situated between the cooling cell and the TOF assembly effectively holds the ions in the cooling cell.

For maXis HD, maXis plus and maXis instruments upgraded with the HDC-cell, a lens system between the collision cell and the TOF assembly holds the ions in the collision cell.

The ions are injected into the TOF by setting the lens voltage to a voltage below the cooling cell bias. Now, the ion beam can overcome the lens potential and can pass through the electrostatic focusing lenses and then into the extraction region of the TOF.

This ion beam is not really as thin as the very thin line shown in Figure 4-2, it has a radial dimension.

Orthogonal Extraction: There are 2 operational states for the orthogonal accelerator:

(i) The **Fill Phase** (injection): The Cooling Cell Exit lens voltage is dropped down to allow the ions to fill the extraction volume. The TOF acceleration voltages are switched off.

(ii) The **Extraction Phase**: The TOF acceleration voltages , i.e. Repeller (push) and Extractor (pull), are switched on to push the ions out of the extraction volume into the flight tube.

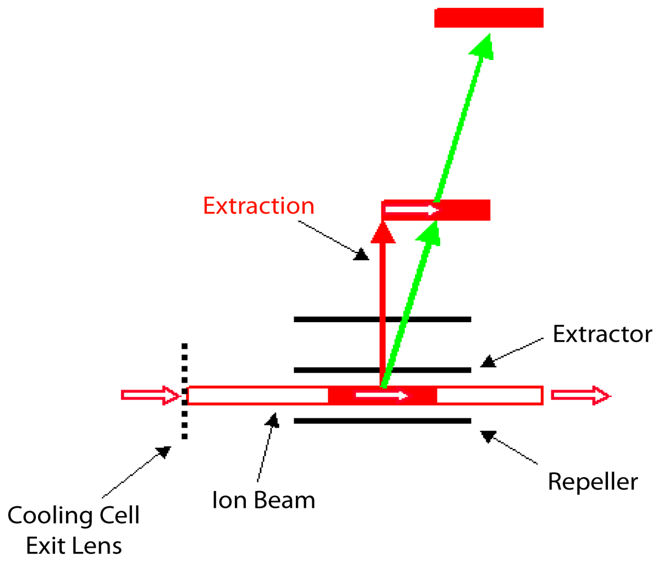


Figure 4-13 Ion beam: injection and extraction in the orthogonal accelerator

The injection velocity and the extraction velocity are added vectorially. Hence, the ions leave the accelerator at an angle $\varphi = \arctan \sqrt{(U_{ext}/U_{inj})}$ which is independent of the ions' mass.

The pulsed injection of the ions from the cooling cell into the accelerator gives rise to a time-of-flight separation in the incident ion beam: The injection energy (Cooling Cell Bias) is converted into kinetic energy ($1/2\ m \cdot v^2$). Hence, the ions' velocity and their arrival time in the extraction volume are dependent on their mass. This has to be considered for the timing (transfer time, pre pulse storage).

4.7.2 Orthogonal TOF: Extraction

When the extraction region of the TOF is filled with the ion beam/bunch, the acceleration voltage is switched on, pushing the ions through the accelerator unit into the flight tube where the ions move uniformly. During the acceleration the ions closer to the repeller plate will get more energy than those farther away.

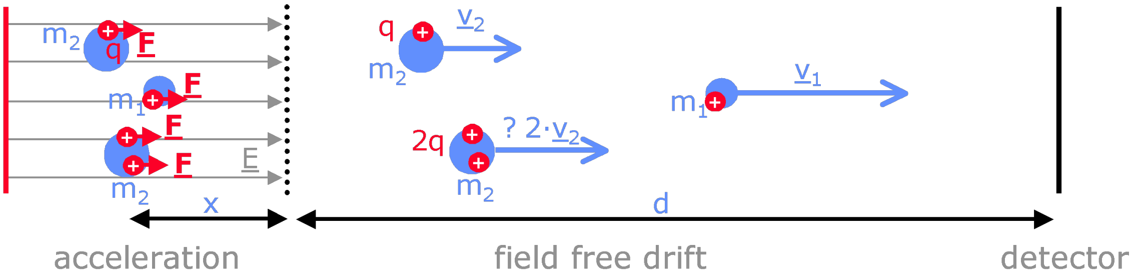


Figure 4-14 Acceleration of ions

$$\underline{a} = q/m \cdot \underline{E} \qquad v = \sqrt{(2 \cdot U \cdot q/m)}$$

$$t_{acc} = 2x \cdot \sqrt{[m/(2 \cdot q \cdot U)]} \qquad t_{drift} = d \cdot \sqrt{[m/(2 \cdot q \cdot U)]}$$

total Time of Flight: $t_{total} = (d + 2x) \cdot \sqrt{[m/(2 \cdot q \cdot U)]}$

effective Flight Path: $d_{eff} = t_{total} \cdot \sqrt{[(2 \cdot q \cdot U)/m]}$

TOF Principle: In the accelerator the ions are accelerated by the electric field, acting on their charge. Hence they get a kinetic energy E = ½ m·v2 which equals their potential energy q·U. U is the local potential at the starting position. In the field free drift the ions fly uniformly until they hit the detector.

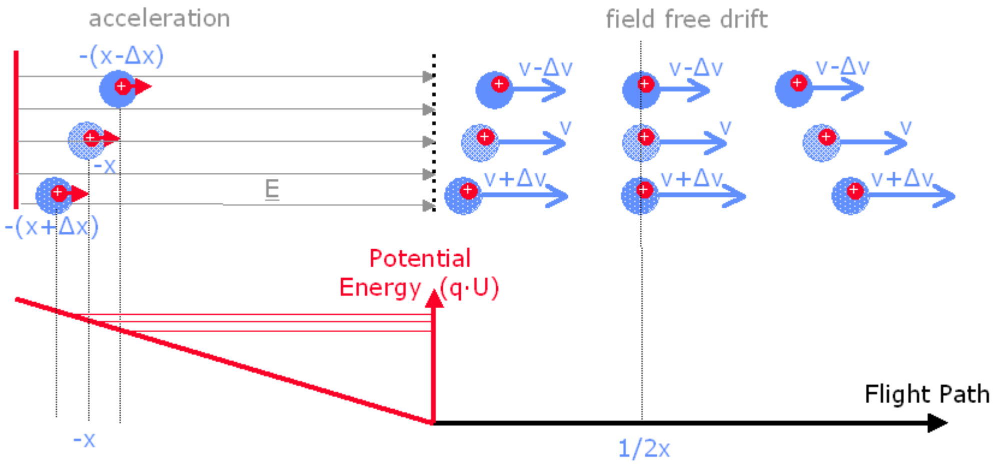


Figure 4-15 **Start and space shift of ions with the same mass**

Depending on their starting position, and hence the local potential, the ions get different energies. Ions starting closer to the repeller plate (left) get more energy, but have a longer flight path. Due to their higher kinetic energy they catch up with the ions starting more to the right, with less energy as well as a shorter flight path, in a first order space focus at ½ x. After the space focus the ions drift apart again, now with the faster ions in front. The reflector will compensate for this difference.

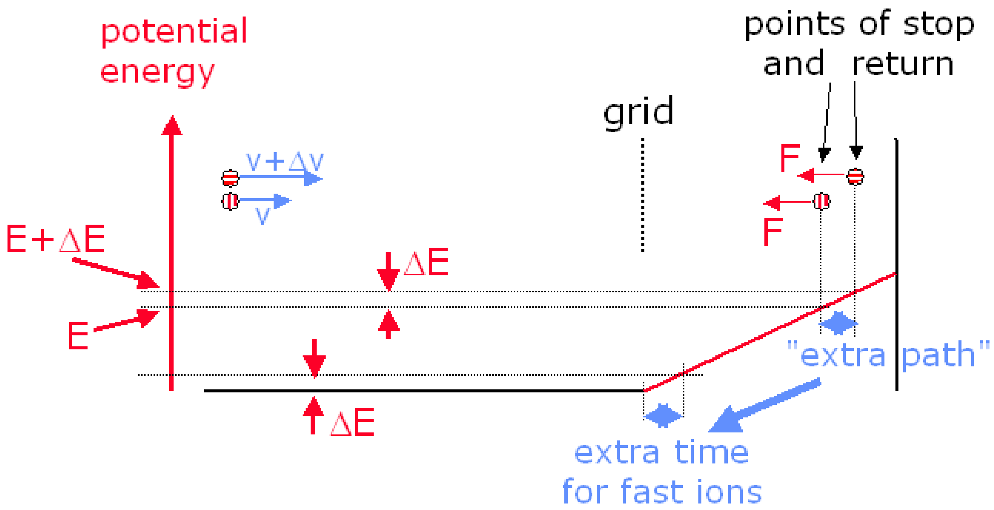


Figure 4-16 **Focusing of ions in the reflector**

In the reflector the ions are retarded, stopped and finally reaccelerated towards the detector. Ions with higher kinetic energy fly deeper into the reflector and spend more time in the retarding field. This effect is used to compensate the shorter flight time of the faster ions in the (field free) flight tube. The compensation is optimized when the ions spend the same amount of time in both the flight tube and the reflector. In terms of distance, the field free flight path should be twice as long as the reflector. This is true for standard, single-stage reflectors. In maXis Series, enhanced dual stage reflection technology is used (see section 2.3.6.4).

5 Maintenance of the maXis Series

This section gives users guidance on regular maintenance that is required to ensure consistent instrument operation.

WARNING

Operators may be exposed to the following during maintenance access:

- Chemical Residues (section 5.1)
- Biological Residues (section 5.2)
- High Temperatures (section 5.3)
- Hazardous Voltages (section 5.4)

5.1 Chemical Residues

The API-Electrospray interface does not ionize all of the sample and solvent! The majority of sample and solvent passes through the interface without being ionized. The vacuum pumps of the maXis Series pump away the unionized sample and solvent. The exhaust from these pumps can contain traces of samples and solvents. Vent all pump exhaust outside or into a fume hood. Comply with your local laws and regulations.

WARNING

The exhaust fumes from the vacuum system and spray chamber will contain trace amounts of the chemicals being analyzed. Health hazards include chemical toxicity of solvents, samples, buffers, and pump fluid vapor, as well as potentially biohazardous aerosols of biological samples. Vent all exhausts outside the building where they cannot be re-circulated by the environmental control systems. Do not vent the exhaust into your laboratory. See the warning labels on the instrument.

WARNING

When replacing pump fluid, use protective gloves and safety glasses. Avoid contact with the fluid.

WARNING

Fluid drained from the spray chamber is composed of solvent and sample from your analyses. The fluid in the mechanical and diffusion pumps collects traces of the samples and solvents. In addition, non-nebulized solvent and sample accumulate at the bottom of the spray chamber. Connect the drain at the bottom of the spray chamber to a closed container. Handle and dispose of all fluid with care appropriate to its chemical and/or biological content. Handle all used pump fluid as hazardous waste. Dispose of used pump fluid as specified by your local laws and regulations. Also refer to the Material Safety Data Sheets (MSDS) obtainable from the supplier.

5.2 Biological Residues

The NanoSpray interface does not ionize all of the sample and solvent. Some sample and solvent passes through the interface without being ionized. The vacuum pumps of the maXis Series are designed to pump away the unionized sample and solvent. The exhaust from these pumps can contain traces of samples and solvents. Vent all pump exhaust outside or into a fume hood. Comply with your local regulations and laws.

WARNING

Fluid drained from the spray chamber is composed of solvent and sample from your analyses. The fluid in the mechanical and diffusion pumps collects traces of the samples and solvents. In addition, non-nebulized solvent and sample accumulate at the bottom of the spray chamber. Connect the drain at the bottom of the spray chamber to a closed container. Handle and dispose of all fluid with care appropriate to its biohazardous and biological content. Handle all used pump fluid as hazardous waste. Dispose of used pump fluid as specified by your local laws and regulations.

WARNING

The needle in the NanoSpray source is extremely thin. Avoid touching it and causing a puncture wound, especially when working with dangerous and toxic substances.

5.3 High Temperatures

Many parts of the maXis Series operate at temperatures that can cause serious burns. These parts include:

• Mechanical pumps	• APPI UV lamp
• Drying gas heater	• Capillary and capillary cap
• Drying gas	• Spray shield
• APCI heater (vaporizer)	

Also exercise care with any other parts that come into contact with the drying gas (the entire spray chamber, capillary, capillary cap and lamp can also present a burn hazard).

Most of these parts are normally covered or shielded. Therefore the covers also become hot. Avoid touching these parts!

WARNING

Many of these parts remain hot for a substantial period of time after the maXis Series has been shut down or switched off. Pay attention when working on a recently shut down instrument to avoid burn injuries.

5.4 Hazardous Voltages

WARNING

Never remove any of the instrument covers while the mass spectrometer is switched on and connected to a power source.

WARNING

Never open the spray chamber while the instrument is in **Operate** or in **Standby** mode.

WARNING

Any interruption of the protective conductor inside or outside the instrument or disconnection of the protective earth terminal could result in an electrical shock. Intentional interruption is strictly prohibited.

When the maXis Series is connected to the mains, hazardous voltages are applied to assemblies, such as:

- Mechanical pumps.
- Transformers and power supplies in the maXis Series cabinet.
- RF generators.
- Drying gas heater.
- APCI heater.
- APCI corona needle.
- APPI UV lamp.
- HV voltage cable (NanoSpray).
- Wiring and cables between these parts.
- High voltage electrodes (capillary and end plate) in the spray chamber.
- Dynode cables.
- Multiplier cables.
- Lens voltage cables.
- Needle (NanoSpray).
- Needle holder (NanoSpray).

5.5 Maintenance Schedule

General maintenance tasks are listed in the table below. Performing these tasks on schedule avoids problems, prolongs system life, and reduces overall operating costs. Keep a record of all system performance characteristics and maintenance operations performed. This will help in detecting deviations from normal operation.

Table 5-1 Maintenance Schedule

Task	Daily	Weekly	Every 12 months	On request
Flush sample path	●			
Clean spray chamber, spray shield, capillary cap, contacts and the tip of the corona needle	●			
Check rough pump fluid level		●		
Check collision gas supply pressure		●		
Check the ventilation air filters on both sides of the instrument				●
Replace rough pump fluid			●	
Replace Nitrogen Gas Filter			●	●
Inspect hoses, power cords, and cables			●	
Empty drain bottle				●
Replace nebulizer needle				●
Clean or replace entire capillary				●
Clean or replace funnel cartridges or lenses (see Maintenance section 5.6.11)				●

5.6 Maintaining the maXis Series

5.6.1 Vent the Instrument

Applying the 

button opens a dialog to set the instrument in a defined mode. Make one of these three choices (Figure 5-1).

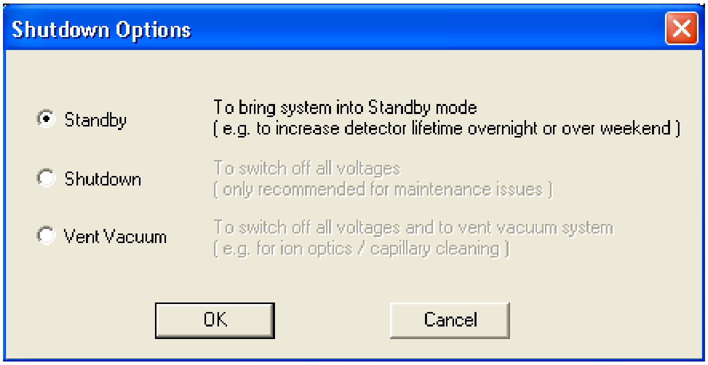


Figure 5-1 Shut down options for the instrument

If you want to vent the instrument click “Vent Vacuum” to select this mode (Figure 5-2)

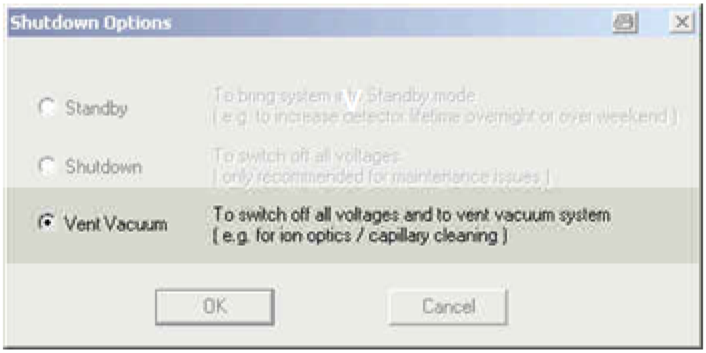


Figure 5-2 Click the "Vent Vacuum" option

A confirmation dialog is displayed as shown in Figure 5-3.

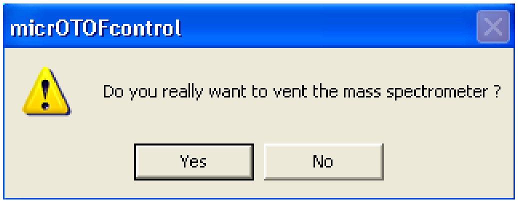


Figure 5-3 Confirmation dialog

Click on “Yes” to vent the instrument.

See the *ESI Standard & APCI Sprayer User Manual (# 8602022)* for further information on the Bruker ESI Sprayer.

5.6.2 Checking Whether the Sprayer is Clogged

The sprayer can be checked by forcing the liquid through the sprayer using the syringe and checking whether it goes through.

WARNING

When checking the sprayer, use protective gloves and safety glasses. Avoid contacting the fluid.

►►To check whether the sprayer is clogged

(1) Open the spray chamber and place a clean, dry cloth inside.

(2) Fill the syringe with solvent.

(3) Carefully push the plunger of the syringe connected to the sprayer and observe whether liquid emerges from the sprayer tip or not.

(4) The sprayer should emit a fine spray when liquid is run through it.

(5) If the sprayer is clogged, refer to section 5.6.4 in the maintenance chapter.

5.6.3 Removing the Sprayer

Maintenance interval

When removing the sprayer for visual inspection or cleaning.

Tools Required

Gloves, latex (# 8200622).

Parts Required

None.

Preparation

Ensure work surfaces are clean and dust free.

WARNING

Sharps and needle hazard. The spray needle tip can puncture latex gloves and skin. Avoid touching the nebulizer tip.

WARNING

Burn hazard. The tip of the sprayer may be very hot. Let it cool down before removing the sprayer.

WARNING

Chemical or Biohazard. Solvents and sample material deposits can be toxic. Take precautions appropriate to the hazard. Read the Material Data Safety Sheets (MSDS) supplied with chemicals.

►►To remove the sprayer

(1) Make sure that the analyte flow has stopped.

(2) Set the heater settings to ambient temperature and wait until the instrument has cooled to ambient temperature.

WARNING

The ESI spray chamber operates at high temperatures. Allow it to cool before proceeding.

(3) Shut off the flow of nebulizing gas.

(4) Open the spray chamber.

(5) Disconnect the LC tubing and nebulizing gas tubing from the sprayer.

(6) Turn the sprayer counterclockwise and disengage it from its retaining screws.

(7) Carefully lift the sprayer out of the spray chamber.

5.6.4 Flushing the Sprayer

Maintenance interval

After a series of measurements, it is recommended that the sprayer, tubing and valves are flushed out with a 50% isopropyl solution.

Tools Required

Isopropyl alcohol, reagent grade or better (# 8058477).

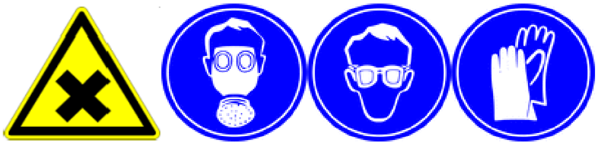
Parts Required

None.

Preparation

Prepare a solution of 50% isopropyl alcohol and 50% water.

WARNING



Isopropyl alcohol is a toxic substance and should be handled with great care. Wear suitable protection equipment. Please refer to the appropriate Material Safety Data Sheet.

►►To flush the sprayer

(1) Remove the sprayer (see section 5.6.3).

(2) Prepare a solution of 50% isopropyl alcohol and 50% water.

(3) Use a syringe and a tube to pump 50% isopropyl alcohol through the sprayer.

(4) Prepare a solution of 50% acetonitrile and 50% water.

(5) Sonicate the sprayer tip in an ultrasonic bath filled with the 50% acetonitrile solution.

Do not allow the sprayer tip to touch the floor or walls of the ultrasonic bath. Ensure that general and local safety laws and guidelines are followed.

(6) Reinstall the sprayer (see section 5.6.8).

Note This procedure can be used for both ESI and APCI sprayers.

5.6.5 Replacing the Sprayer Needle Unit

A clean and undamaged sprayer needle is essential to achieve good electrospray conditions. Flush the sprayer needle before and after each analysis (see section 5.6.4). Flushing helps to keep the sprayer needle clean and reduces the frequency of sprayer needle replacement.

If the needle is damaged, the complete needle unit must be replaced. Do not attempt to disassemble the needle unit.

Important: Never touch the sprayer needle with bare hands. Wear protective gloves.

Maintenance interval

- When the spray needle is visibly bent or damaged.
- When the spray is not symmetrical with the needle assembly.
- When the spray needle is blocked. Common symptoms are increased LC backpressure, off-axis spraying, or dripping from the sprayer.

The spray needle must be replaced when data shows excessive noise or the current signal is unstable.

Tools Required

Gloves, latex (# 8200622)

Wrench 3-mm, open-end (# 8222971)

Wrench 8-mm (# 8032169)

Parts Required

Needle Unit Spare, ESI Sprayer (# 8600632) or Needle Unit Spare, APCI Sprayer (# 8601794)

Preparation

All working surfaces should be clean and dust free

►►To replace the sprayer needle unit

(1) Remove the sprayer from the spray chamber (see section 5.6.3).

(2) Unlock the damaged needle unit by turning the needle unit lock knurl counter-clockwise until it stops.

(3) Grip the zero dead-volume union and turn the needle unit counter-clockwise until the needle unit comes loose.

(4) Hold the sprayer with the tip pointing upwards. This allows debris to fall out of the sprayer shaft before the new needle unit is inserted.

(5) Remove the damaged needle unit. Gentle pulling may be required to overcome the friction of the inner O-ring.

(6) Carefully insert the new needle unit into the sprayer. If resistance is encountered, pull the needle unit back a short distance before continuing insertion.

CAUTION

Be very careful when inserting the needle. The tapered end of the needle must pass through restrictions in the sprayer shaft. The end of the needle can be damaged if it is forced.

(7) Adjust the sprayer needle extension as described in section 5.6.6.

5.6.6 Adjusting the Sprayer Needle

►►To unlock the needle unit for adjustment of the sprayer needle

- Turn the needle unit lock knurl counterclockwise until stop.

►►To lock the Sprayer Needle in position

- Turn the needle unit lock knurl clockwise until finger-tight.

►►To extend or retract the sprayer needle

- Grip the zero dead-volume union and turn the entire needle unit clockwise (to extend needle) or counter-clockwise (to retract needle).

Important: the entire needle unit should rotate. The zero dead-volume union should not be loosened.

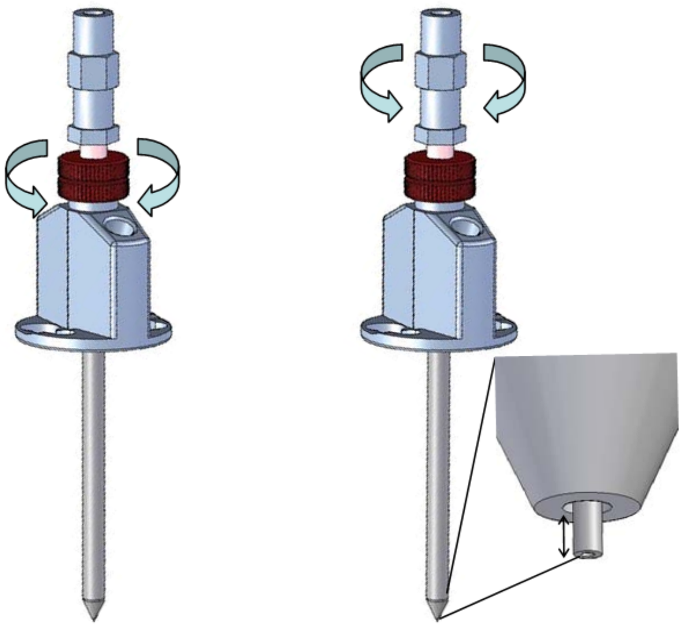


Figure 5-4 Unlocking and locking the needle unit (left) and fine-adjustment of the sprayer needle extension (right)

5.6.7 Fine-Adjustment of the Sprayer Needle

Use the inspection and adjustment fixture and microscope supplied with the sprayer for inspection and fine adjustment of the sprayer needle. The microscope can be mounted on the front or on top of the inspection fixture, enabling the sprayer tip to be inspected from the side or from above.

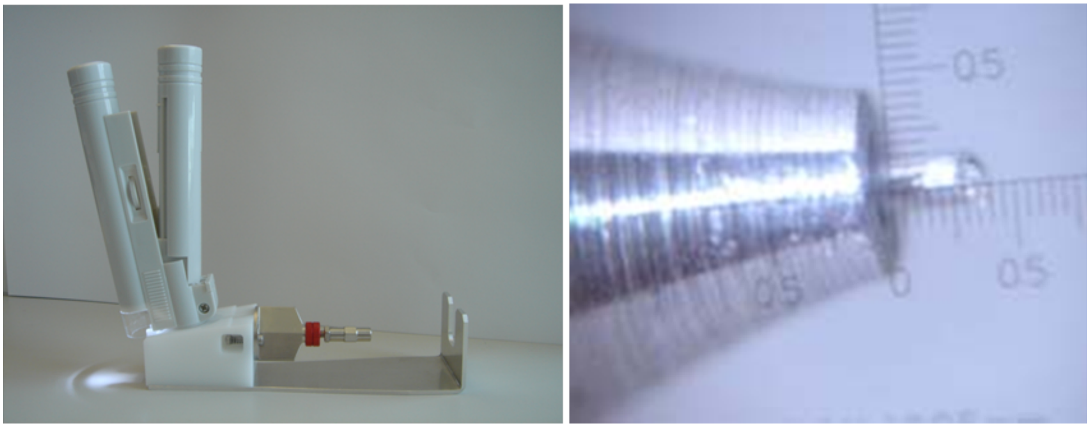


Figure 5-5 Left: Sprayer mounted in the adjustment fixture. Right: Scale on the microscope objective lens for measuring sprayer needle extension

Parts required

Adjustment fixture (# 8020207)

Preparation

All working surfaces should be clean and dust free

►►To adjust the Sprayer Needle

(1) Open the microscope to switch on the light.

(2) Adjust the needle as described in section 5.6.6.

(3) Use the scale on the microscope objective lens (Figure 5-5) to measure the sprayer needle extension.

For optimum performance, the needle can also be fine-adjusted during operation.

5.6.8 Reinstalling the Sprayer

Make sure the nebulizer needle is correctly adjusted. Make sure the spray chamber is open.

►►To reinstall the sprayer

(1) Carefully insert the shaft of the sprayer into the source chamber through the hole in the center of the adapter.

CAUTION

Be careful not to knock the tip of the needle while inserting the nebulizer. The tip of the needle is easily damaged.

(2) Reconnect the nebulizing gas tubing to the sprayer.

(3) Lock the sprayer into position by aligning the large holes in the sprayer retaining plate with the retaining screws on the adapter and turning the sprayer clockwise until it locks into position (see Figure 5-6).

Tighten the two retaining screws if required.

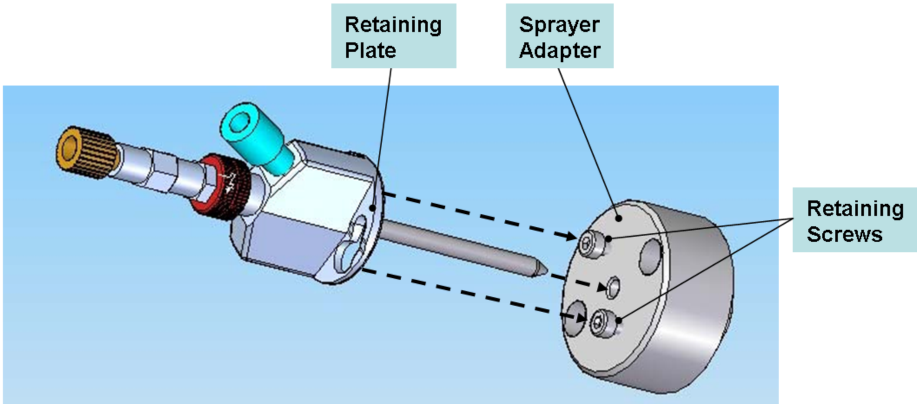


Figure 5-6 Mounting the sprayer onto the spray chamber adapter

(4) Turn the sprayer clockwise to lock it into place.

(5) Reconnect the LC tubing to the zero-dead-volume union.

CAUTION

Do not over tighten the LC fitting. This can crush the tubing, or create a restriction.

(6) Close the spray chamber.

(7) Set the nebulizing gas flow and heater settings to the desired operating values.

5.6.9 Removing the Glass Capillary

When required

Removing the capillary is necessary for cleaning and replacement.

Tools required

Required tools:

- Gloves, chemical-resistant, clean, powder-free, lint free (# 8268095)

Parts required

- Glass capillary (500µm) (# 8027329)

Preparation

- All working surfaces to be clean and dust free.

Procedure

WARNING

The spray chamber operates at very high temperatures. Let it cool down before proceeding.

(1) Vent the maXis Series (see section 5.6.1).

(2) Open the spray chamber.

(3) Remove the spray shield.

(4) Remove the capillary cap from the end of the capillary.

(5) Carefully pull the glass capillary straight out of the desolvation assembly.

CAUTION

Pull the capillary straight out along its long axis. The capillary is made of glass and can break during handling!

5.6.10 Cleaning the Spray Chamber

When Required

It is recommended that the spray chamber is cleaned after each series of measurements to avoid a carry-over of sample material between analyses.

Tools required

- None.

Parts required

- Cloths, clean, lint free (# 8045485).
- Gloves, chemical-resistant, clean, powder-free, lint free (part no. 8268095).
- Isopropyl alcohol 99.5%, reagent grade or better (# 8058477).
- Water, reagent grade or better (# 8049145).

Preparation

- All work surfaces to be clean and dust free.

Procedure

(1) Mix a solution of 50% isopropyl alcohol and 50% water.

WARNING

The spray chamber operates at high temperatures. Let it cool down to ambient temperature before you continue working.

(2) Shut down the instrument (section 5.6).

(3) Remove the Nebulizer (section 5.6.3).

(4) Open the spray chamber.

(5) Dampen a clean cloth with the mixture of isopropyl alcohol and water.

(6) Remove spray shield and capillary cap.

(7) Put both parts into a solvent bath and clean them with an ultrasonic cleaner.

Note If contamination or discoloration of the spray shield and capillary cap cannot be removed by polishing, the use of abrasives may be necessary (see section 5.6.12).

(8) Reinstall the capillary cap and spray shield.

(9) Wipe all other accessible surfaces. Pay special attention to the bottom of the spray chamber near the drain hose and to areas that are discolored.

(10) Close the spray chamber.

(11) Reinstall the Electrospray nebulizer.

5.6.11 Maintenance of Funnel and Multipole Cartridge

When required

- As necessary

Tools Required

- Torx Screwdriver (T6, T8, T10, T20)
- Allen Key

Parts required

- Cloths, clean, lint free (# 8045485).
- Gloves, chemical-resistant, clean, powder-free, lint free (# 8268095)
- Isopropyl alcohol 99.5%, reagent grade or better (# 8058477),
- Water, reagent grade or better (# 8049145).

Preparation

- All work surfaces to be clean and dust free

CAUTION

The funnels and the multipole in the cartridge are very sensitive parts! Be careful to avoid damaging them!

5.6.11.1 Disassembling and Cleaning Multipole Cartridge and Funnel

(1) Vent Vacuum System

Follow the venting process detailed in Section 5.6 and wait until the system is totally vented.

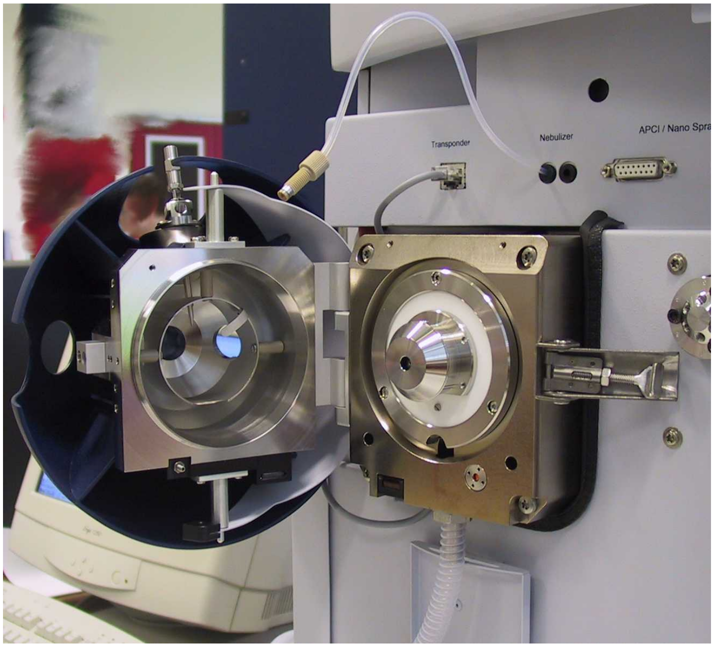
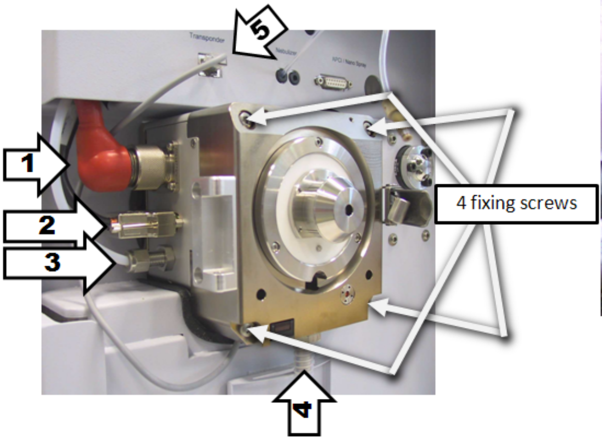


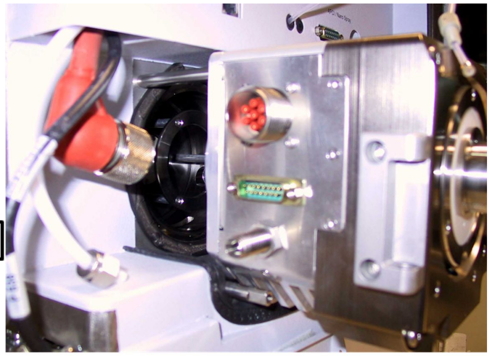
Figure 5-7 Ion source open

(2) Remove Ion Source

Disconnect the tubing from the Nebulizer and remove the Spray Chamber by unclipping the toggle clamp on the right-hand side, swinging the chamber to 90° and lifting it off its pivot pins.

(3) Remove Desolvation Unit





Pull out desolvation unit

Figure 5-8 Disconnect cables and tubing; unscrew the four fixing T20 screws

(4) Remove the cartridge containing the funnels and the multipole

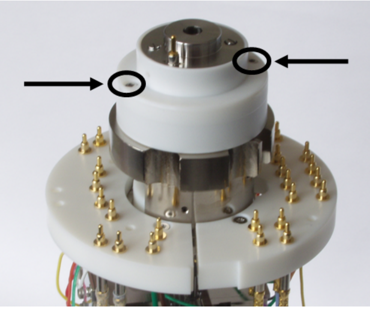
a. Locate the multipole cartridge

b. Hook your fingers inside the metal Grab Handle and pull to break the double seal.

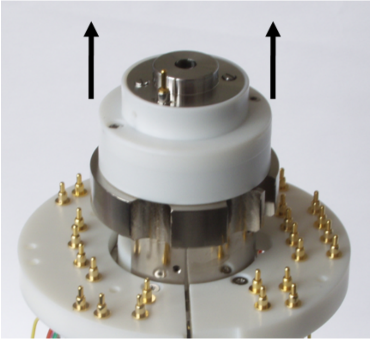
c. Ease the cartridge out of the instrument and transfer it to the bench

(5) Reassemble the Desolvation Unit to protect the vacuum system from contamination.

(6) Remove Lens Block.

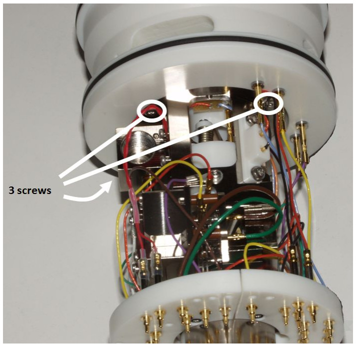


a. Remove two Torx T10 screws securing the Lens Block to the transfer cartridge.

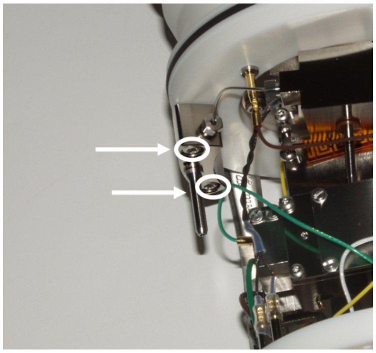


b. Ease the Lens Block off. This can be a very tight fit and may require gentle leverage.

(7) Remove Funnel 2.



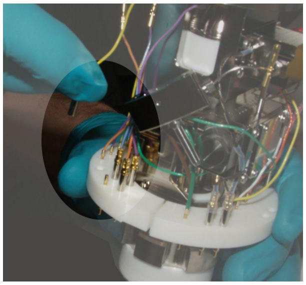
a. Remove three Torx T10 screws securing Funnel 2 to the transfer cartridge.



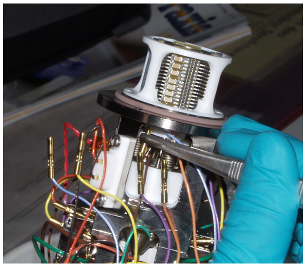
b. Remove two Torx T10 screws from gas inlet.

c. Disconnect 5 wires and separate the two sub-assemblies.

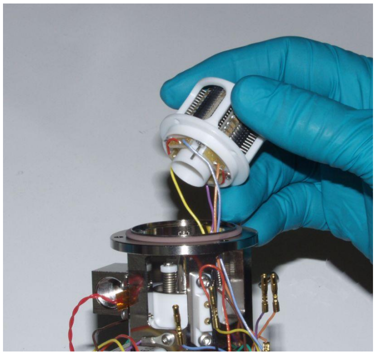
d. Remove four further Torx T8 screws securing the funnel.



e. Disconnect the four Funnel 2 wires.



f. Disconnect brown cable from underside of Funnel 2 using tweezers.

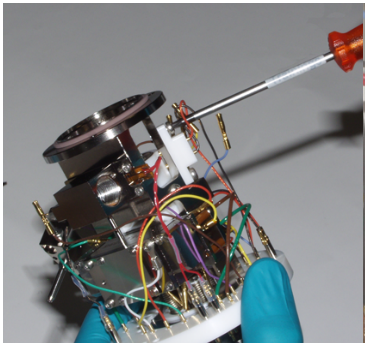


g. Remove Funnel 2.

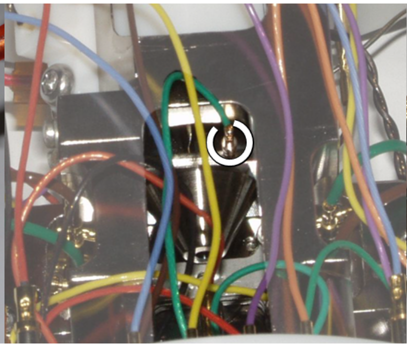
(8) Cleaning Funnel 2

The complete funnel can be washed with acid-free organic solvents in an ultrasonic bath.

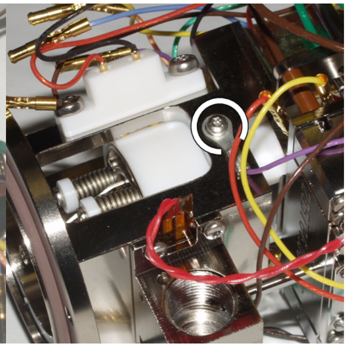
(9) Removal of Multipole 1



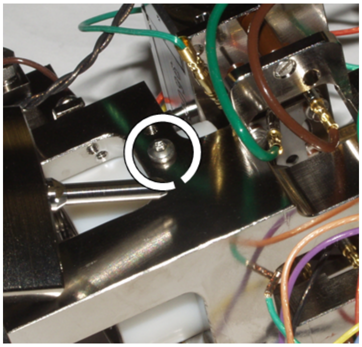
a. Remove two Torx T10 screws from the multipole connector and pull connector out.



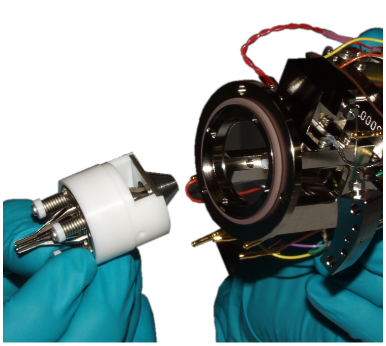
b. Disconnect the green wire from the inside end of the multipole.



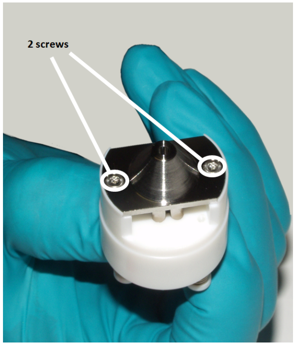
c. Unscrew T6 retaining screw also releasing purple wire ring tag.



d. Turn assembly over and remove T6 screw from opposite side of assembly.



e. The multipole can then be removed from the assembly.

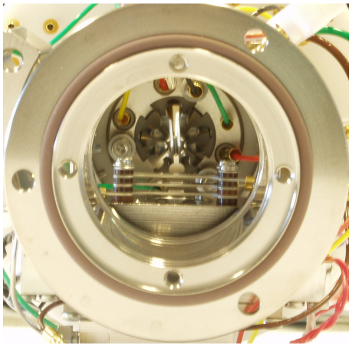


f. The multipole subassembly can be further dismantled by removing two screws

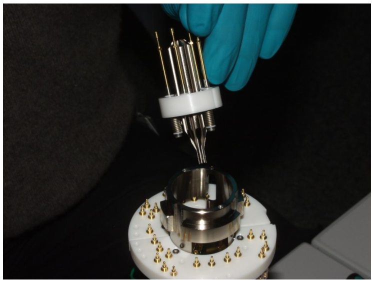
(10) Cleaning Multipole 1

The components of the multipole can be washed with acid-free organic solvents in an ultrasonic bath.

(11) Removal of Multipole 2



a. The wires on the underside of multipole 2 can be seen through the bore of the cartridge.



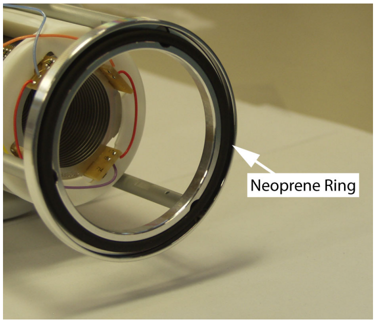
b. Using tweezers, disconnect the wires and slide multipole 2 out from the transfer cartridge.

c. Multipole 2 is now ready for cleaning.

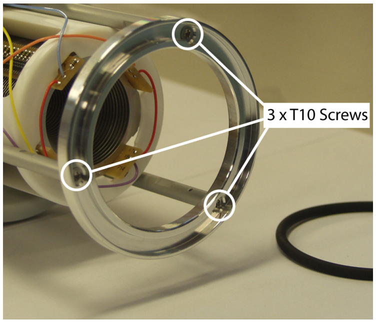
(12) Cleaning Multipole 2

The multipole can be washed with acid-free organic solvents in an ultrasonic bath.

(13) Remove the Grab Handle

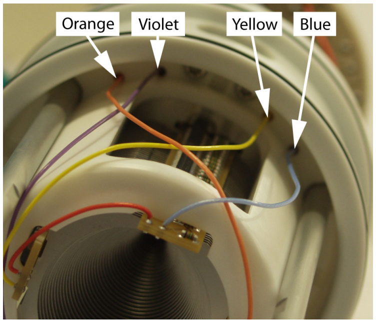


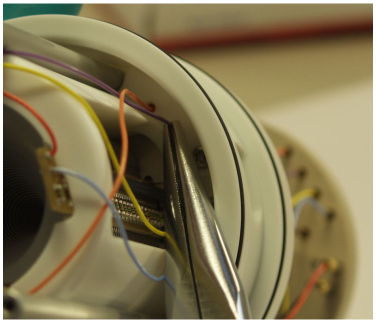
a. Remove the neoprene ring with tweezers.



b. Remove the Grab Handle by unscrewing the three Torx T10 screws.

(14) Disconnect Funnel 1 wiring.

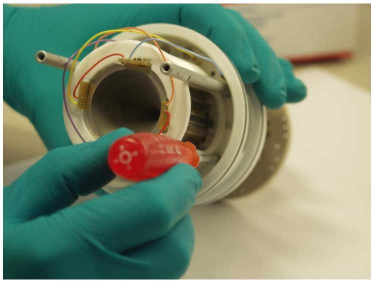


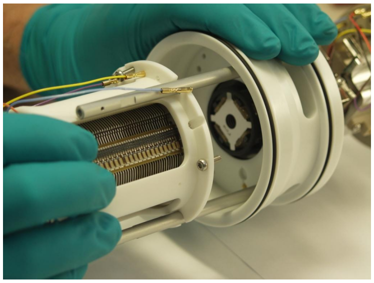


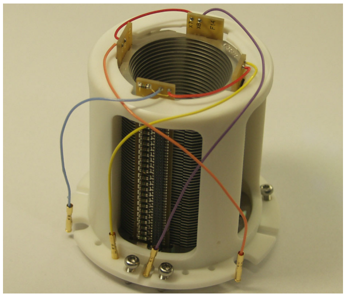
a. The four wires connecting Funnel 1 must be disconnected from their sockets in the transfer cartridge.

b. Use narrow nosed pliers to ease the connectors from the sockets.

(15) Unscrew Funnel 1.







a. Four Torx T10 screws secure the Funnel 1 to the transfer cartridge

b. Remove these screws. Funnel 1 then pulls straight out.

c. Funnel 1 is now ready for cleaning

(16) Cleaning Funnel 1

The complete funnel can be washed with acid-free organic solvents in an ultrasonic bath.

NOTE

Do **not** use acidic solvents to clean any part of the product or its components.

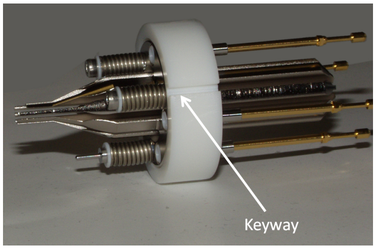
After manual cleaning, funnel 1, funnel 2, the Multipoles and the Lens block must be cleaned in an ultrasonic cleaner with appropriate solvents.

5.6.11.2 Re-Assembling Multipole Cartridge Lens Block and Funnels

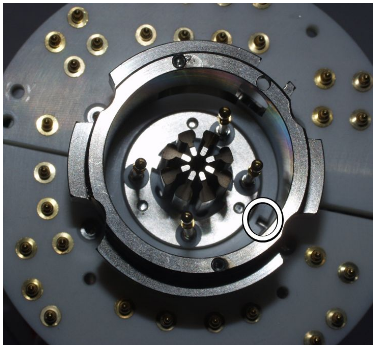
Generally, reassembly is the reverse of the dismantling procedure.

(1) Reassembling Multipole 2

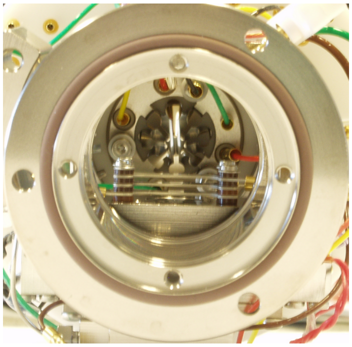
Both multipole must be oriented correctly in the multipole cartridge. The molding on Multipole 2 has a keyway detail shown in Figure (a) below. This keyway must be aligned with the pin inside the multipole cartridge as shown in Figure (b) below.



a. The Multipole 2 showing the keyway



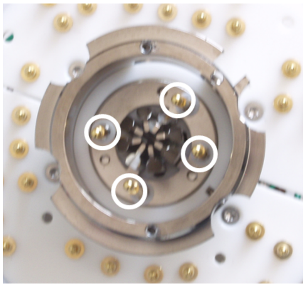
b. Position of the location pin in the bore of the cartridge.



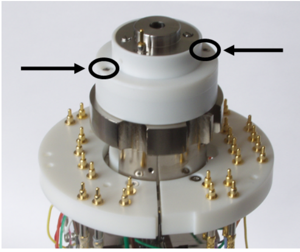
c. With the Multipole in place, reconnect the wires by sighting along the bore.

(2) Reassembling the Lens Block

a. Ensure that the orientation of the lens block is correct. Inside of lens block shown here

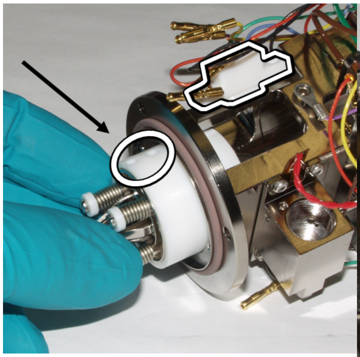


b. The four pad positions must align with the pins on the multipole.

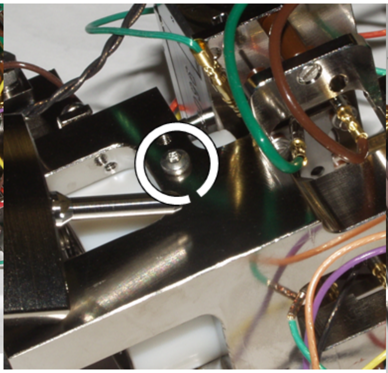


c. Replace the two Torx T6 screws

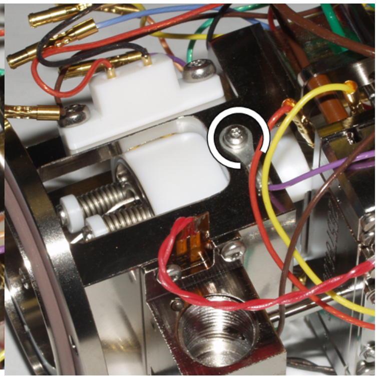
(3) Reassembling multipole 1



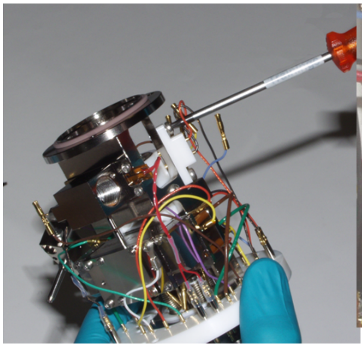
a. Align the two contact pads with the multipole connector and push the multipole into the bore.

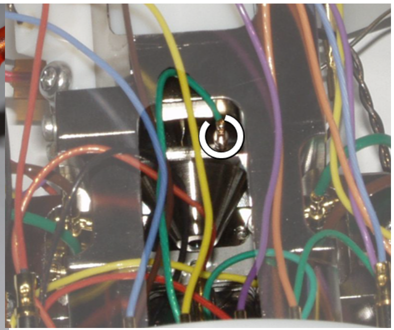


b. Holding the multipole in position, turn the assembly over and insert the T6 screw but do not tighten fully.



c. Turn the assembly over again and insert the second T6 screw with the ring terminal and tighten both screws.

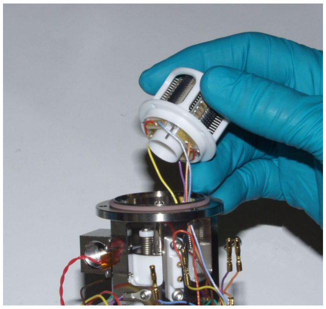


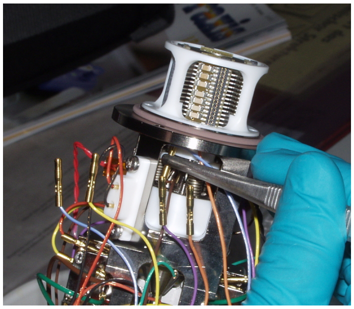


d. Position the multipole connector and push it down to compress the spring contacts. Insert and tighten down two T10 screws.

e. Reconnect the green wire using tweezers.

(4) Reassembling Funnel 2

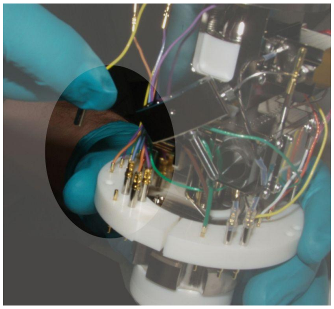




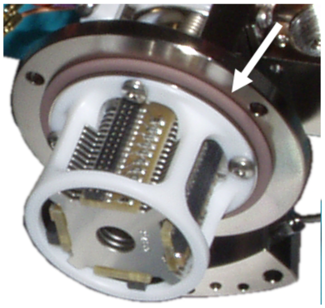
a. Feed wires through the side apertures and line up Funnel 2 with the screw holes.

b. Replace four Torx T8 screws. Do not tighten fully until all four screws are inserted.

c. Reconnect brown wire on underside of Funnel 2 using tweezers.

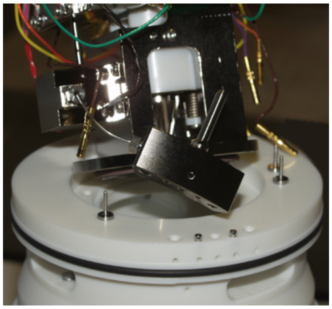


d. Reconnect the four Funnel 2 wires.

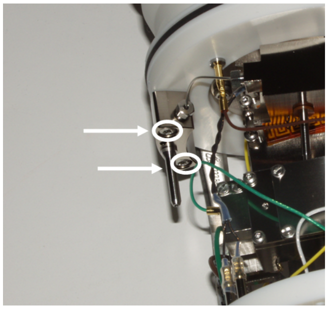


e. Check sealing ring for damage.

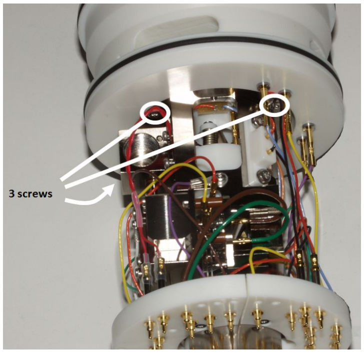
f. Replace the Funnel 2 and Multipole subassembly onto the cartridge.



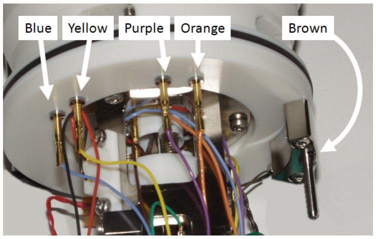
g. Line up the gas inlet with the locating dowels.



h. Replace two Torx T10 screws and tighten.

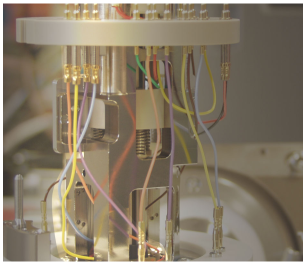


i. Replace three Torx T10 screws. Tighten fully when all three are inserted.

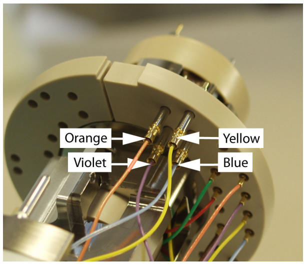


j. Reconnect 5 wires.

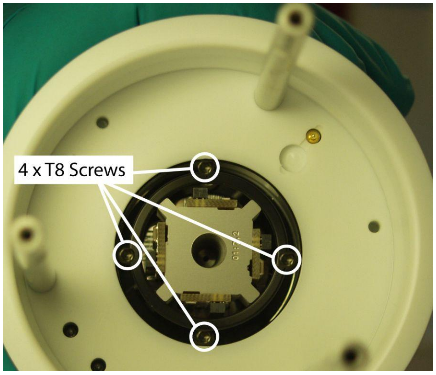
(5) Reassembling Funnel 1



a. Feed the Funnel 2 wires through the apertures in the transfer cartridge.



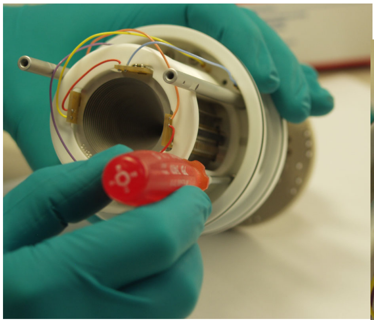
b. Plug wires into the correct sockets.



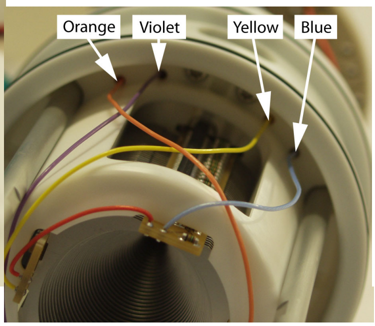
c. Position four Torx T8 screws in Funnel 2 screw-holes, lower Funnel 2 into the recess and tighten down the screws.

(6) Reassembling Funnel 1

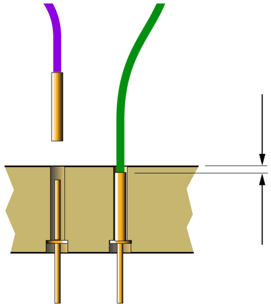
Funnel one has only one possible assembly position because of the screw positions. Fasten with four Torx T10 screws and relocate the wires into the correct sockets in the transfer cartridge. The connectors should be pushed sub-flush to ensure a good connection.



a. Use four Torx T10 screws to secure Funnel 1 to the transfer cartridge.



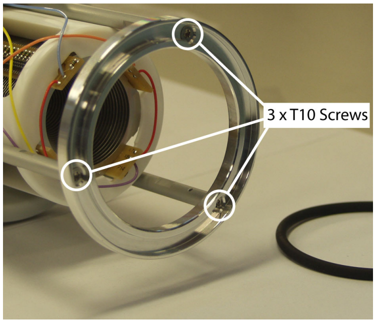
b. Plug wires into the correct sockets.

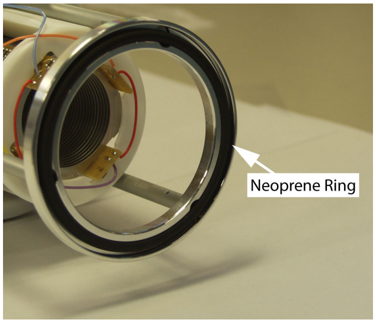


c. Ensure that the female connectors are pushed sub-flush to ensure a secure contact.

(7) Refitting the Grab Handle

The Grab Handle and the neoprene O-ring are essential to ensure positive connection between the Multipole Cartridge and the connector pads in the transfer stage.





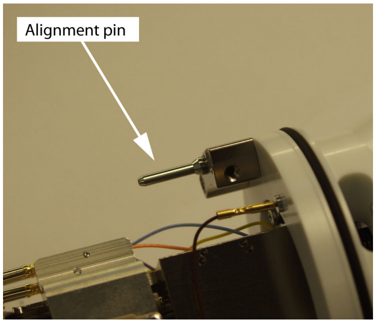
a. Use three Torx T10 screws to attach the Grab Handle to the three spacer bolts.

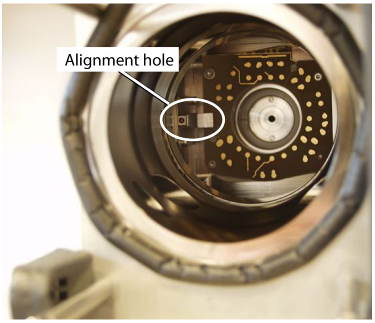
b. Fit the neoprene O-Ring into the annular groove.

5.6.11.3 Re-fitting the Multipole Cartridge to the maXis Series

(1) Installation of the Multipole Cartridge

The multipole cartridge uses an alignment pin to ensure that the contact pads in the Ion Transfer Stage casing connect with the spring connectors on the multipole assembly (see below).





a. The alignment pin is mounted on the edge of the Multipole Transfer cartridge

b. The alignment hole can be found on the left-hand side of the Transfer-Stage cavity

Push the Multipole Cartridge into the Transfer Stage cavity, ensuring that the pin is located in its socket.

(2) Install Desolvation Unit and Source Chamber

There is a neoprene O ring fitted to the rear side of the desolvation unit. This O-ring is critical in maintaining a vacuum inside the maXis Series. Before installing the desolvation unit, ensure that the O-ring is properly seated in the annular groove. Even a small displacement of the O-ring can result in it being damaged.

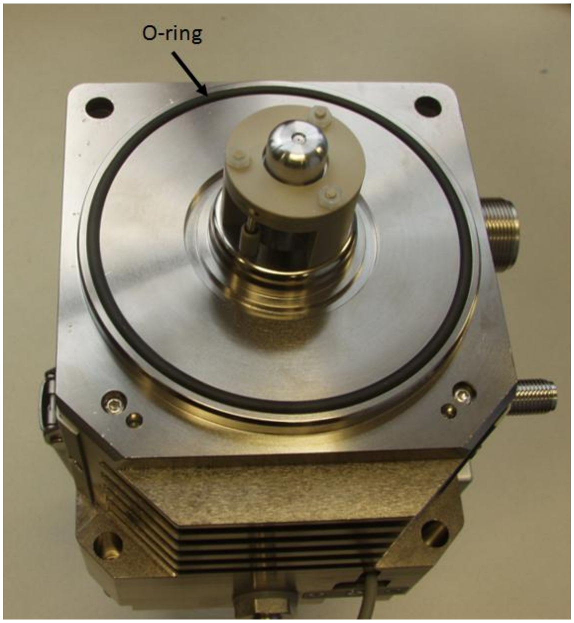


Figure 5-9 Desolvation unit showing the O-ring correctly fitted.

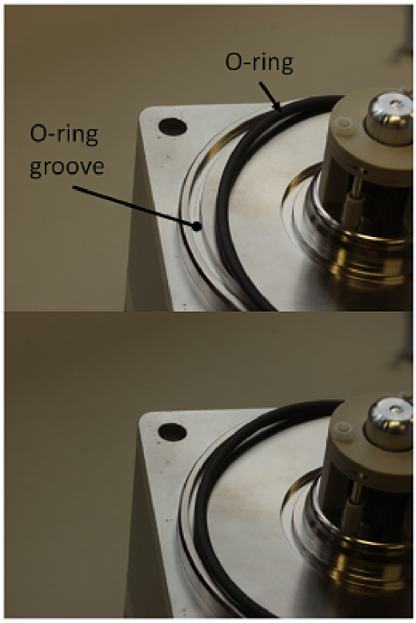


Figure 5-10 Desolvation unit with O-ring displaced from groove.

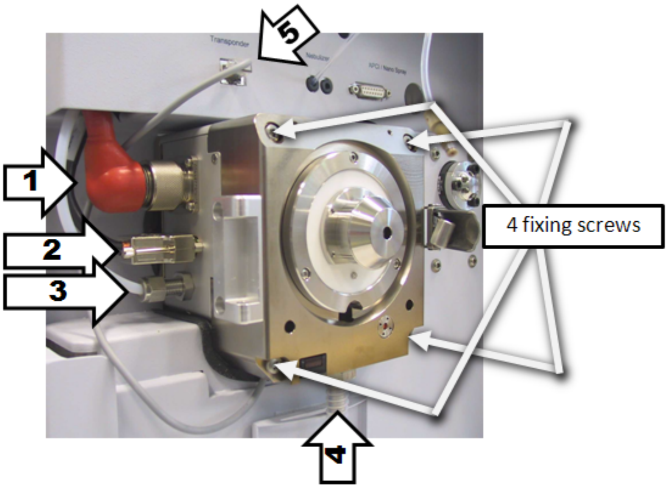


Figure 5-11 **Connect cables and tubing, insert and tighten down 4 fixing screws**

a. Slide the desolvation unit into position and connect the cables and tubing (see Figure 5-11).

b. Insert the four fixing screws and tighten them securely.

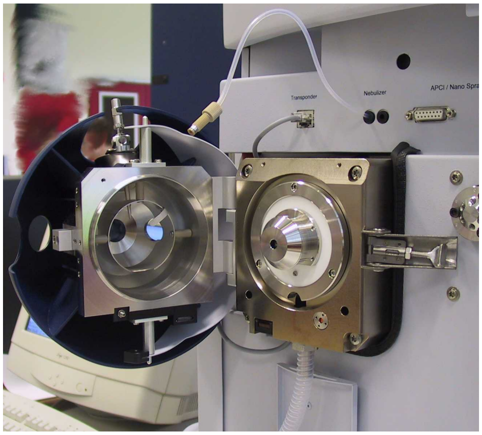


Figure 5-12 **Replace the spray chamber**

- Replace the spray chamber by sliding it onto the hinge pins in the open position (see Figure 5-12). Close the chamber and lock it in place using the toggle clamp.

(3) Pump vacuum system

In the otofControl software click on ‘Standby’ . A confirmation dialog will appear, asking ‘Do you really want to….’. Click ‘YES’. and the vacuum pumps will start to evacuate the system.

5.6.12 Abrasive Cleaning

When required

Abrasive cleaning of the spray shield or capillary cap will be necessary if significant discoloration or deposits cannot be removed by polishing.

Tools required

- Sand paper, 8000 grit,
- Cloths, clean, lint free (# 8045485),
- Gloves, chemical-resistant, clean, powder-free, lint free (part no. # 8268095)
- Isopropyl alcohol 99.5%, reagent grade or better (# 8058477),
- Water, reagent grade or better (# 8049145).

Parts required

None.

Preparation

Make a cleaning solution (50% [v/v] isopropyl alcohol) by mixing equal volumes of isopropyl alcohol and water.

All work surfaces should be clean and dust fee.

CAUTION

Because the spray shield and capillary cap are made of stainless steel, they can safely be abraded. However, these are the only parts that should be cleaned in this way. Many other metal parts, such as the spray chamber, may look similar to stainless steel, but are made of much softer metals or are plated with materials that will be damaged by abrasive cleaning.

WARNING

The spray chamber operates at high temperatures. Let it cool down to ambient temperature before proceeding.

(1) Shut down the maXis Series (section 5.6).

(2) Open the spray chamber.

(3) Remove the spray shield.

(4) Remove the capillary cap.

(5) Place the sandpaper grit side up on the workbench.

(6) Move the flat surface of the spray shield over the surface of the sandpaper in a figure of 8. Only the large flat surface needs to be cleaned in this way unless there are obvious deposits elsewhere on the shield. Use a Cotton-Tipped Applicator and mixture of isopropyl alcohol and water to clean the inner rim of the main hole in the spray shield.

(7) Clean the capillary cap with the sand paper. Only the end surface of the cap needs to be cleaned in this way unless there are obvious deposits elsewhere on the shield. The inner rim of the hole in the cap may occasionally need cleaning.

(8) Put the capillary cap into a solvent bath and clean it with an ultrasonic cleaner.

(9) Reinstall the capillary cap.

(10) Reinstall the spray shield.

(11) Close the spray chamber.

5.6.13 Replacing the Nitrogen Gas Filter

When required

Replacing the Nitrogen gas filter is necessary when it is saturated and chemical background appears when other sources of chemical background, such as solvents and spray chamber contamination, can be excluded. If ions are present and no sample or solvent is flowing, this is also an indicator that the Nitrogen Gas Filter requires replacement.

Tools required

- Wrench, 1/2 x 9/16-inch, open-end.

Parts required

- Nitrogen Gas Filter, (# 8219454).

Preparation

- None.

Procedure

(1) Shut down the maXis Series (section 5.6).

(2) Turn off the gas flow at its source.

(3) Remove the old Nitrogen gas filter by unscrewing the unions.

(4) Connect the Pipe from the nitrogen source to the inlet of the new Nitrogen Gas Filter.

(5) Turn on the flow of nitrogen gas at its source.

(6) Purge the filter for 5 minutes at the normal pressure.

(7) Turn off the flow of nitrogen gas at its source.

(8) Connect the pipe from the outlet of the gas conditioner to the maXis Series.

(9) Turn on the gas flow at its source.

(10) Dispose of the old filter in accordance with the instructions on the Material Data Safety Sheet (MSDS)

5.6.14 Replacing the Ventilation Filters

When required

Replacing the ventilation filters is necessary when they become clogged with dust and they prevent the free flow of ventilating air. The life of a filter will depend on the environment in which the instrument operates. For this reason, it is important to check the filters on a monthly basis.

Tools required

- No tools required.

Parts required

- Replacement filter x2, (# 8260994).

Preparation

- Have the replacement filters ready to install. Operating the instrument without ventilation filters can cause the performance of the instrument to deteriorate.

Procedure

(1) Remove the ventilation grilles on both sides of the instrument base (see Figure 5-13). The grilles each have two latches which should be pushed down (Figure 5-14).

(2) Pivot the grille as shown in Figure 5-15and pull the grille upwards to release the three tabs on the lower edge of the grille.

Figure 5-13 Position of ventilation grille and latches

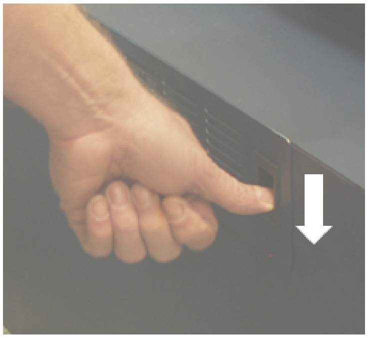


Figure 5-14 Push latches down to release grille

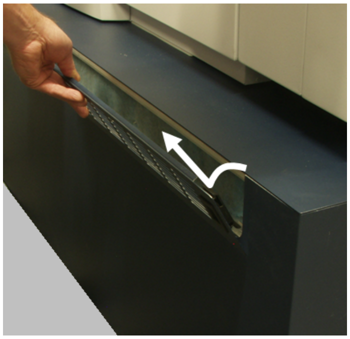


Figure 5-15 Pivot grille out and pull upwards

(3) Pull the old filter material from the keeper tabs and dispose of it.

(4) Push the new filter material into place ensuring that it is located behind the keeper tabs.

(5) Replace the grille by first locating the three tabs along the lower edge into the slots in the instrument housing. Pivot the grille inwards to engage the latches. The latches may need to be pushed down to engage properly with the instrument housing.

5.7 nCI related Maintenance (ETD Option only)

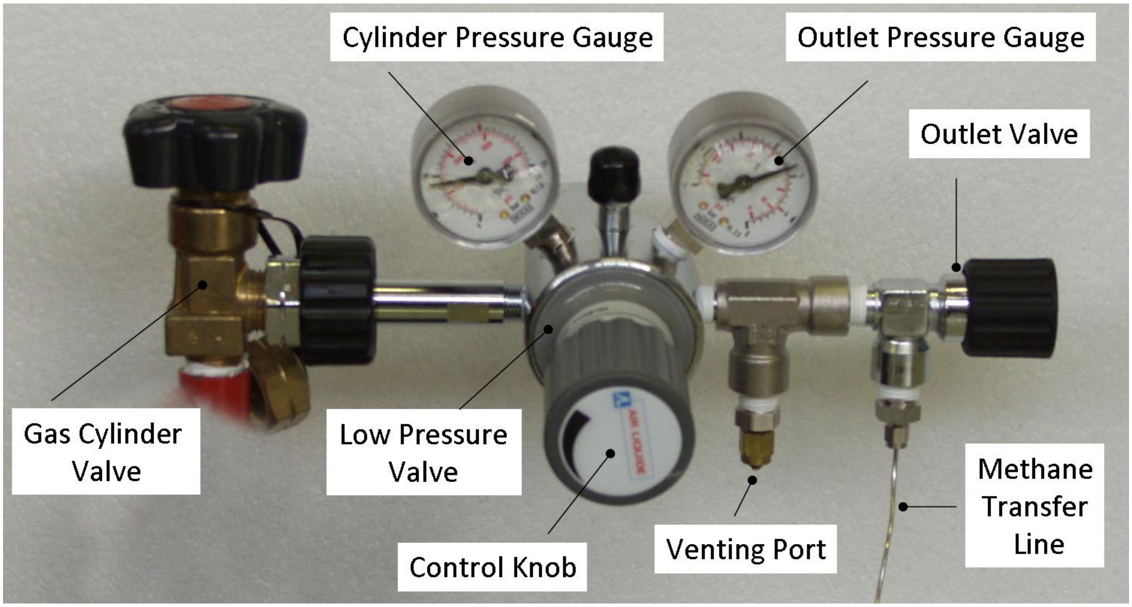


Figure 5-16 Typical methane two-stage pressure regulator

WARNING

Methane is extremely flammable and can form explosive mixtures with air.

Keep containers in a well-ventilated area.

Keep away from ignition sources.

Take precautionary measures against static discharge.

5.7.1 Replacing the Methane Gas Cylinder

The methane gas cylinder should be replaced before the methane pressure (displayed in the cylinder pressure gauge, see 1.3.4) drops to ambient pressure.

Methane must be supplied at a minimum quality of 5.0 (99.999 % purity).

The maximum volume of methane gas cylinders used with the maXis Series instrument is 2 liters. Use of larger volume cylinders is prohibited.

A two-stage pressure regulator with a venting port is required to supply methane from pressurized gas cylinders (see 1.3.4) according to specifications that can be found in the Site Preparation Document.

Before replacing the methane gas cylinder, familiarize yourself with the precautions to be taken when using methane for operating the CI source (see section 1.3.4).

The following procedure must be performed according to your local regulations.

Consult your local facility safety representative for advice on replacing pressurized methane gas cylinders.

Refer to the Material Safety Data Sheet (MSDS) provided by your methane gas supplier.

If in any doubt, refer to your local regulations and to the requirements of the local facility safety representative.

WARNING

Methane is extremely flammable and can form explosive mixtures with air.

Keep containers in a well-ventilated area.

Keep away from ignition sources.

Take precautionary measures against static discharge.

Procedure

(1) Close the regulator outlet valve.

(2) Close the methane gas cylinder valve.

(3) Adjust the pressure regulator control knob to the lowest possible value to separate the low-pressure stage from the high-pressure stage.

(4) Disconnect the old methane gas cylinder from the regulator.

(5) Connect the new methane gas cylinder to the regulator. Refer to requirements of your gas cylinder supplier.

(6) Open the methane gas cylinder valve for as long as is necessary to fully pressurize the inlet stage of the pressure regulator. Close the valve of the methane gas cylinder immediately after the inlet stage is fully pressurized.

To prevent ambient air diffusing back into the gas cylinder, opening the cylinder valve for long periods should be avoided.

The pressure indicated by the pressure gauges should not drop after closing the cylinder valve.

If the pressure drops, there is a leak that must be remedied before this procedure can be continued (see section 5.7.2).

(7) Adjust the pressure regulator control knob to 4 bar at the low-pressure stage.

(8) Slightly open the venting port to allow methane to exhaust. Close the venting port before the inlet pressure (displayed on the cylinder pressure gauge) drops below 10 bar.

Note Only perform the venting procedure described in step 8 if the venting port of your regulator is connected to an exhaust in compliance with local and national regulations. Otherwise proceed to step 10.

(9) Repeat steps 6 to 8 twice.

(10) Check for leaks using the procedure described in section 5.7.2.

If no leaks are present, open the methane gas cylinder valve and adjust the outlet pressure to 4 bar using the regulator knob.

(11) Close the gas cylinder valve.

(12) Close the regulator outlet valve.

5.7.2 Checking for Leaks in the Methane Supply and Transfer Line

The methane supply and transfer line must be checked regularly for leaks (see maintenance schedule, (section 5.5).

Perform the following procedure after each exchange or reconnection of a methane cylinder (see section 5.7.1), after installation of the methane supply or re-connection of the instrument to the methane line, or after any alteration of the methane supply or to the connection between methane supply and instrument.

This procedure requires a methane supply outlet with a low-pressure stage that can be evacuated along with the outlet pressure gauge. The outlet pressure gauge must be able to indicate pressure values of 1 bar below ambient pressure.

Installation of a back-flash protection valve in the methane transfer line may prevent the procedure from running properly.

(1) Make sure the ETD nCI-source is switched off in the instrument-control software and that the source flush option (for venting the Methane Line) is not activated. (ETD dialog)

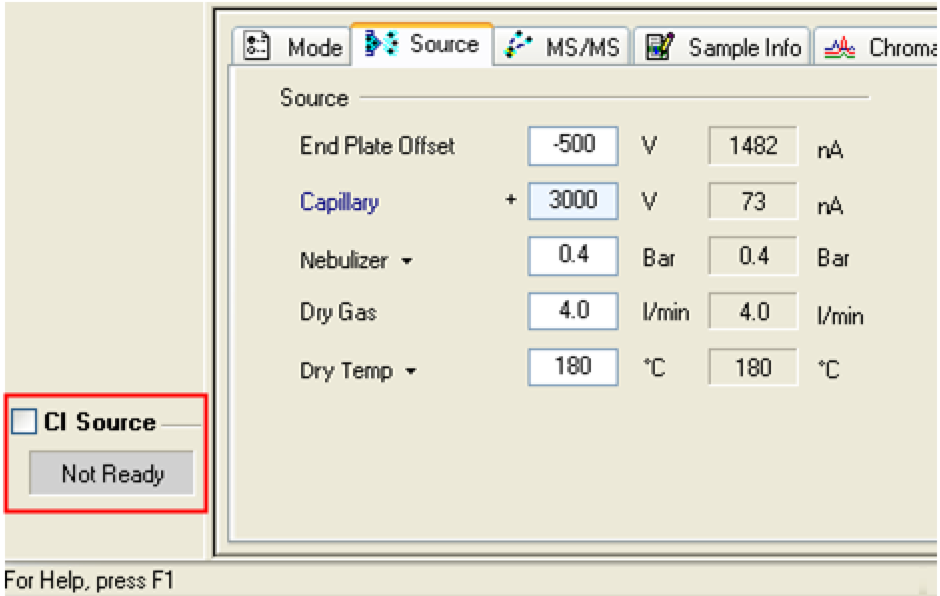
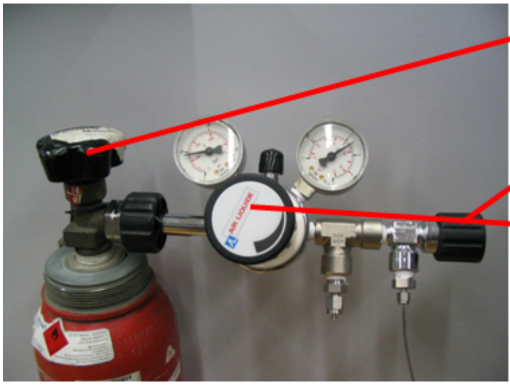


Figure 5-17 CI Source flush option

WARNING

Excessive opening of the methane bottle main valve should be avoided before a leak test has been performed.



- Close the main valve of the methane bottle if not already done.
- Close the methane supply outlet shut-off valve.
- Close the flow into the low-pressure stage of the methane supply outlet.

Figure 5-18 Methane valve details

(2) Close the main valve of the methane bottle if not already closed.

(3) Close the methane supply outlet shut-off valve.

(4) Close the flow into the low-pressure stage of the methane supply outlet.

(5) Check the reading on the high-pressure stage.
The pressure in the high-pressure stage of the methane supply, as indicated by the pressure gauge, should not drop appreciably. If it does, there is a leak between the methane bottle and the regulator which must be remedied.

(6) Check the reading on the low-pressure stage.
The pressure in the low-pressure stage of the methane supply, as indicated by the pressure gauge, should not drop appreciably. If it does, there is a leak between the regulator and the shut-off valve which must be remedied.

(7) Open the methane supply outlet shut-off valve.
The pressure indicated by the pressure gauge may drop slightly while opening the shut-off valve but should not continue to drop afterwards. If it does, there is a leak in the transfer line between the methane supply and the methane inlet valve inside the instrument which must be remedied.

(8) Activate the source flush option (for venting Methane Line) in the instrument-control software (CI Source dialog).
The pressure indicated by the pressure gauge should drop slowly.

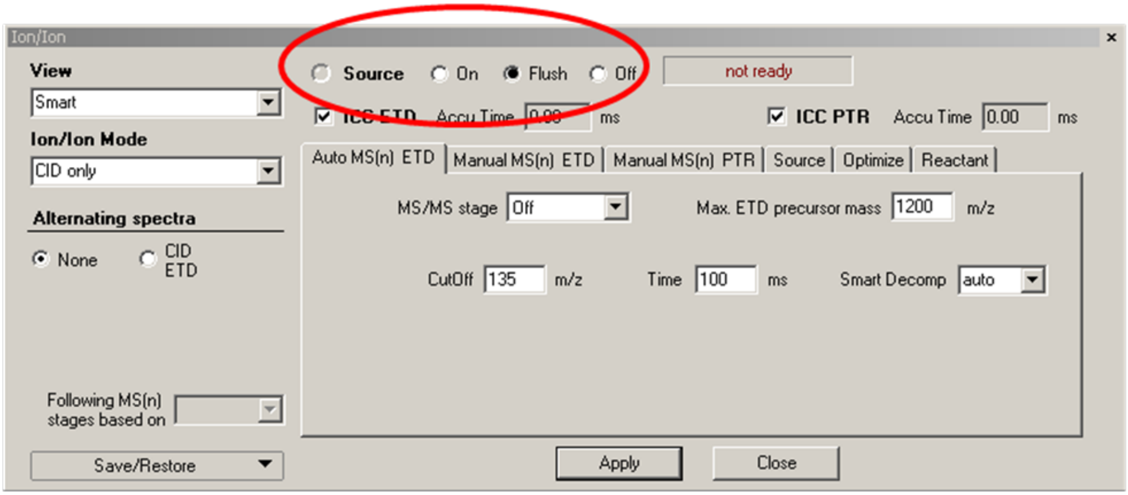


Figure 5-19 Source flush option acivated

(9) If a gas bottle with pressure regulator is used, adjust the low pressure to ca. 2.5 bar.

(10) Slightly open the venting port to allow methane to exhaust.

(11) Close the venting port before the inlet pressure drops below 10 bar.

(12) The pressure in the high-pressure stage must drop before the pressure in the low-pressure stage starts to drop. This may take several hours.

(13) If the pressure indicated by the gauge does not drop at all, check

- whether the methane valve inside the instrument is audibly switching when disabling and enabling “Flush”

- whether the main valve of the methane bottle is not completely closed
- whether the stainless steel methane capillary is plugged

(14) The pressure indicated by the gauge must drop below zero (to approximately -1 bar below ambient).

Where the gauge is able to indicate pressure values below ambient and the indicated pressure stays at ambient pressure, there is a leak between the methane gas bottle and the pressure regulator or the stainless steel methane capillary to the instrument, which must be remedied.

It can take several hours to see the pressure drop below ambient; therefore the test should be conducted overnight.

5.7.3 Replacing the Disposable Reagent Cartridge

Tools Required

- Gloves, chemical-resistant, clean, powder-free, lint free (# 8268095)
- Slot-head screwdriver
- Wrench 14-mm, open-end

The reagent being used for ETD should last between 6 months and 1 year depending on the level of usage.

For directions on how to exchange the reagent cartridge please contact BDAL – Service.

The instrument must be vented and disconnected from the mains before replacing the disposable reagent cartridge. See Section 5.6 for details of the venting process.

The disposable reagent cartridge is located inside the instrument. To access the cartridge, two covers must be removed.

Procedure to remove a used Reagent cartridge:

(1) Follow the venting process detailed in Section 5.6 and wait until the system is totally vented.

(2) Familiarize yourself with the Material Safety Data Sheet (MSDS) for the reagent material.

(3) Switch off the main switch and disconnect the power cable from mains.

(4) Double-check that the instrument is disconnected from the mains before proceeding.

Figure 5-20

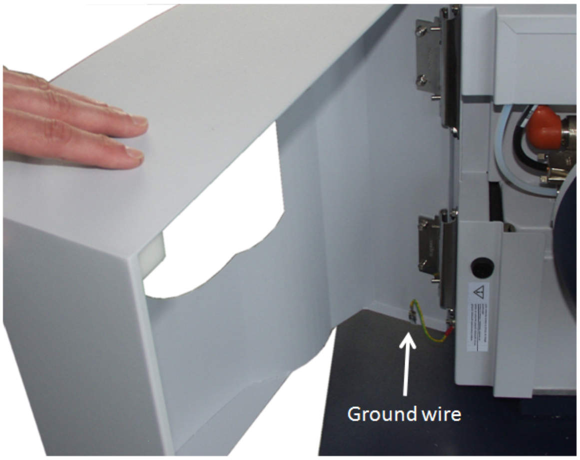


Figure 5-21

(5) Open the hinging front cover (Figure 5-20) and disconnect the ground wire (Figure 5-21). Please note that the spade connector has a locking tab (Figure 5-22) that must be pressed to release the connector. Unclip the hinges by retracting the hinge pins (Figure 5-23 and Figure 5-24) and set the cover aside.

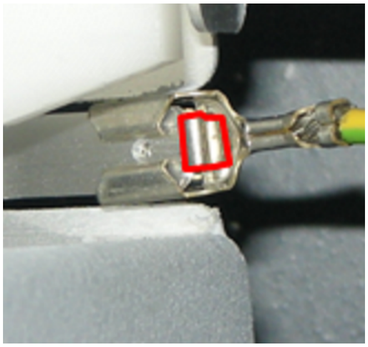


Figure 5-22

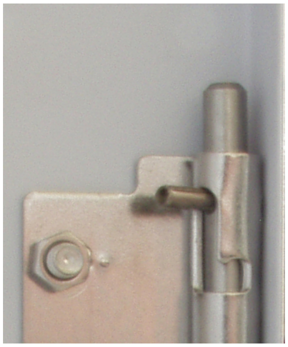


Figure 5-23

Figure 5-24

(6) The inner cover is held in place by two latches on either side of the instrument (Figure 5-25). Turn these counterclockwise (Figure 5-26) with a broad-blade slot screwdriver.

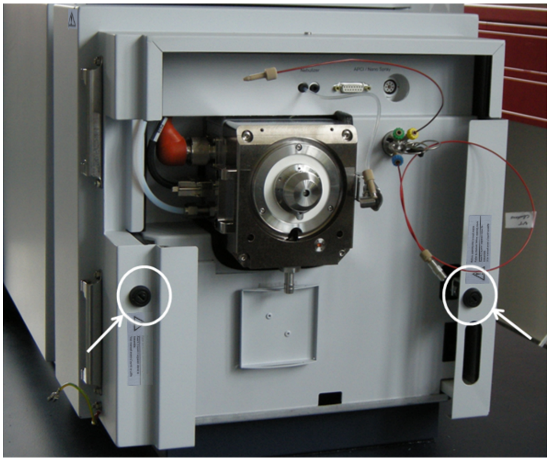


Figure 5-25

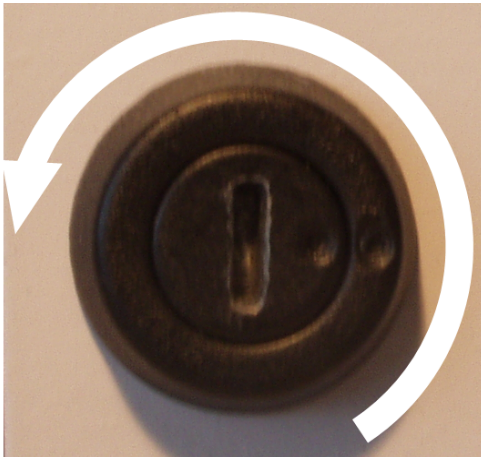


Figure 5-26

(7) Slide the cover out on its rails for about 15 cm (6 in) (Figure 5-27) and disconnect the ground cable from the inner front cover. This is located on the right-hand side of the instrument. Please note that the spade connector has a locking tab (Figure 5-28) that must be pressed to release the connector.

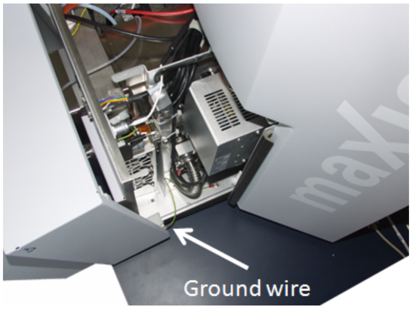


Figure 5-27

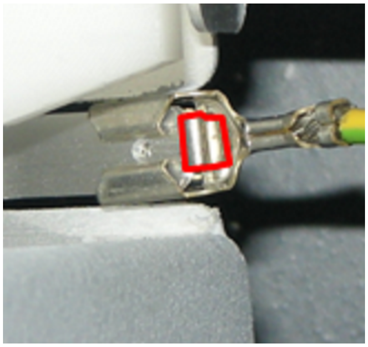


Figure 5-28

(8) Set the inner cover aside.

(9) The reagent cartridge is now accessible on the left hand side of the instrument (Figure 5-29)

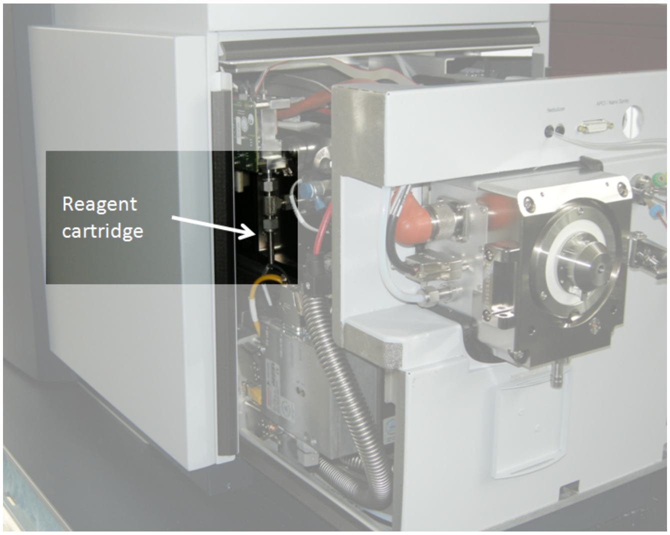


Figure 5-29

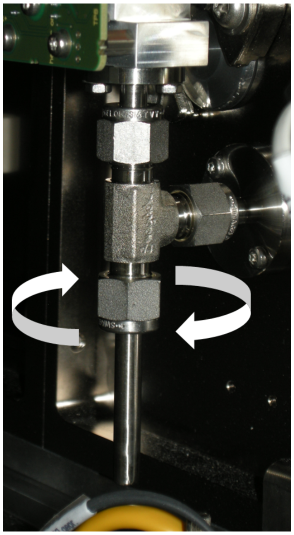
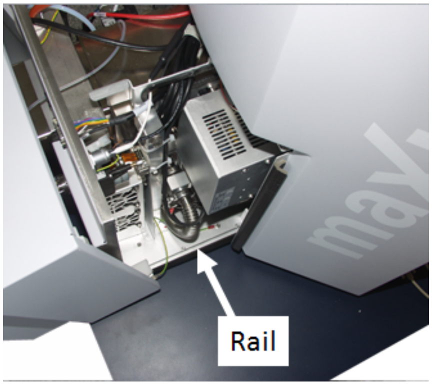


Figure 5-30

(10) Loosen the lower nut on the TEE (Figure 5-30) to remove the reagent cartridge from the instrument.

(11) Slide the new cartridge fully into position in the TEE and tighten the nut carefully until it is finger tight. Use a wrench to tighten the nut a further ¼ turn.

(12) Dispose of the cartridge as directed in the Material Safety Data Sheet (MSDS).



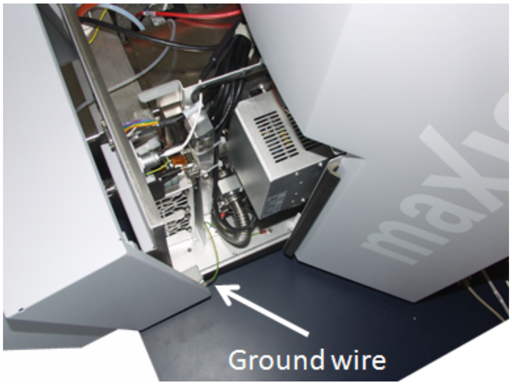
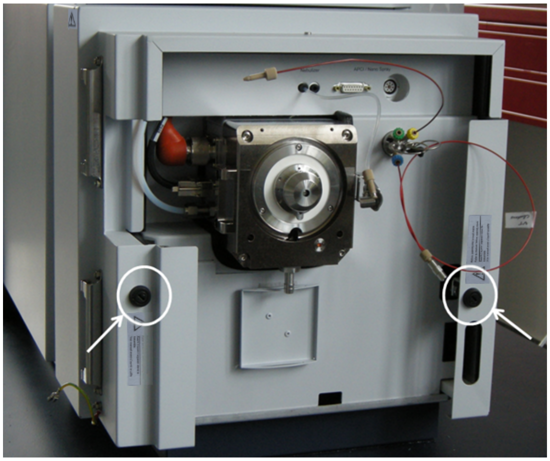


Figure 5-31

Figure 5-32

(13) Position the inner cover on the rails of the bottom of the instrument (Figure 5-31) and reconnect the ground wire (Figure 5-32).

(14) Push the inner cover along the rails until it meets the end stop. Turn the latches clockwise to lock the inner cover in place (Figure 5-33 and Figure 5-34).



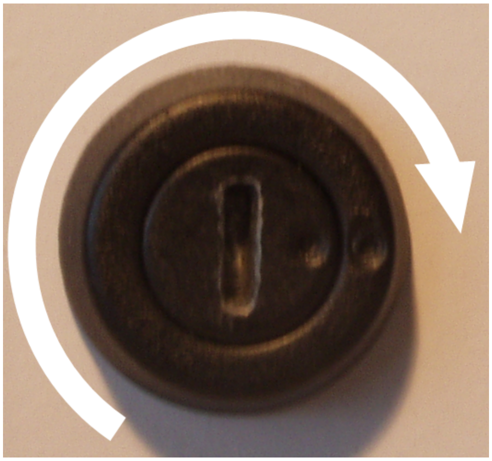


Figure 5-33

Figure 5-34

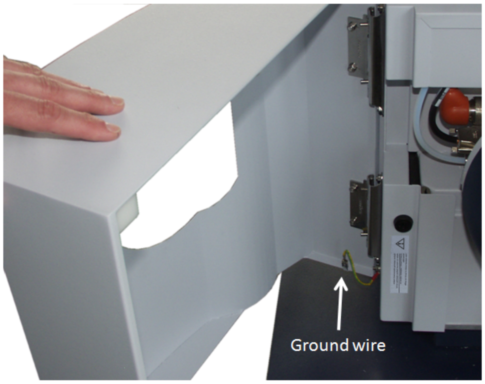


Figure 5-35

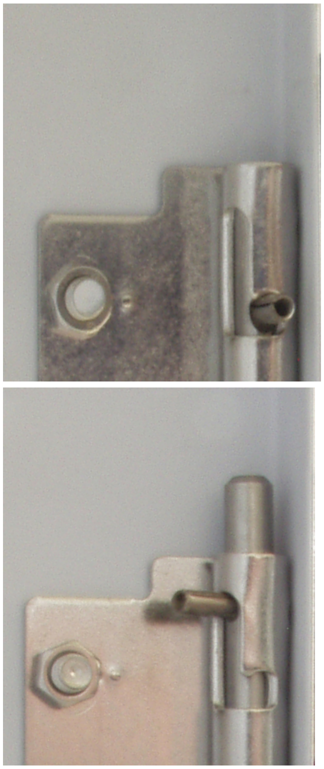


Figure 5-36

(15) Position the front cover and unlatch the hinge-pins (Figure 5-35 and Figure 5-36).

(16) Reattach the ground wire (Figure 5-35) and close the cover.

(17) Reconnect the instrument with the mains and switch it on again.

(18) Conduct a leak test as described in section 5.7.4.

5.7.4 Leak Check for the Reagent Cartridge

When the instrument is ready again, perform the following procedure:

1. Flush the nCI source for 5 minutes.
2. Load the method ETD-Reagent_tune.m.
3. Switch on the nCI source and activate the Reagent Mode.

   The only visible signals should be those from azulene at around *m/z* = 128.2 and 129.2 (see Figure 5-37). No tungsten oxide clusters should be visible at around *m/z* = 230.

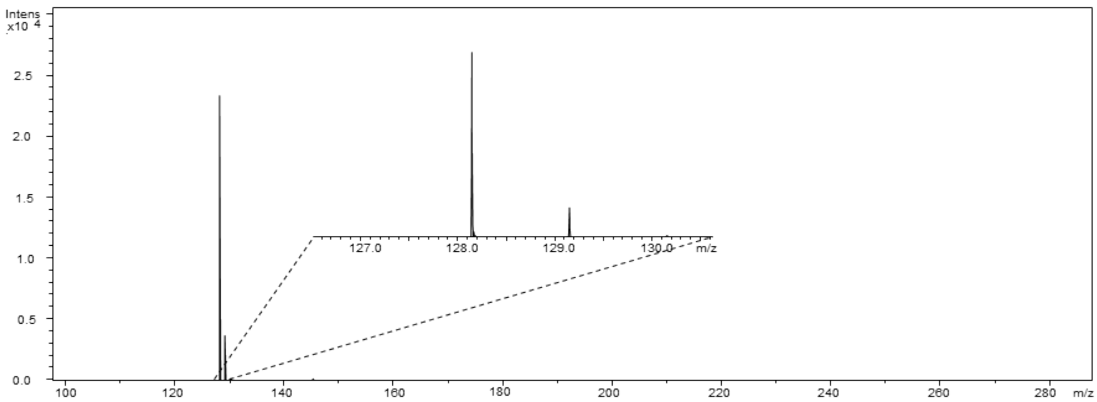


Figure 5-37 Reagent anion signal after replacing the Disposable Reagent Cartridge (no tungsten oxide clusters are detectable)

4. If tungsten oxide anion clusters are observed (see Figure 5-38), switch off the nCI source immediately.
   a. Vent and switch off the instrument, and disconnect the power cable from the mains.
   b. Proceed with steps 3–9 of the procedure in section 5.7.3.
   c. Tighten the nut by another ¼ turn and proceed with steps 13–18 of the procedure in section 5.7.3.

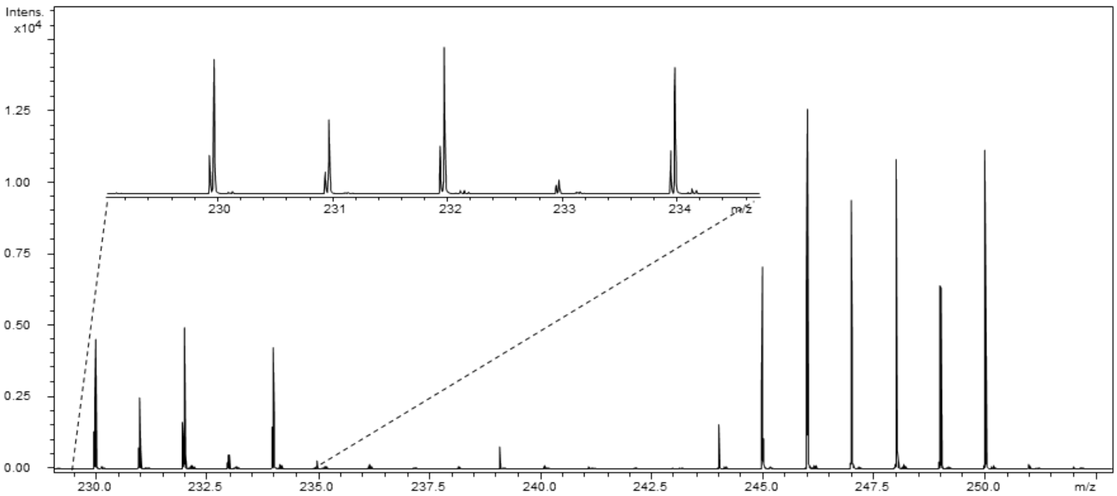


Figure 5-38 Tungsten oxide anion cluster at m/z 230, the inset shows the isotopic pattern for tungsten clusters having one tungsten atom.

Appendix A — Spare Parts and Schematics

A.1 List of Spare Parts

Description	Part No.
Carbon Filter	# 8219454
Air Filter Pad	# 8216264
Desolvation Unit	# 8216221
Spray shield	# 8210036
Capillary Cap	# 8216156
Contact spring (Gold plated)	# 8073046
Glass Capillary (500 µm)	# 8027329
ESI-Source (without sprayer)	# 8218063
Sprayer	# 8020210
Sprayer Needle (ES shipping kit)	# 8027281
APCI-Source	# 8021568
Nebulizer APCI	# 8024623
Sprayer needle APCI	# 8073032
APCI Corona needle	# 8072569
APP-Source	# 8212978
Roughing pump (Varian DS602)	# 8218818
Oil, Inland 45 for Rough Pump	# 8020221
Exhaust Filter	# 8218820
Oil exhaust replacement cartridge	# 8226181
Tools	
3 mm wrench	# 8222971
8 mm wrench	# 8032169

Description	Part Number
Torx T-25	# 8217352
Magnifier	# 8020206
Sprayer Adjustment fixture	# 8020207
Syringe Pump	# 8046866

A.2 Schematic of the maXis

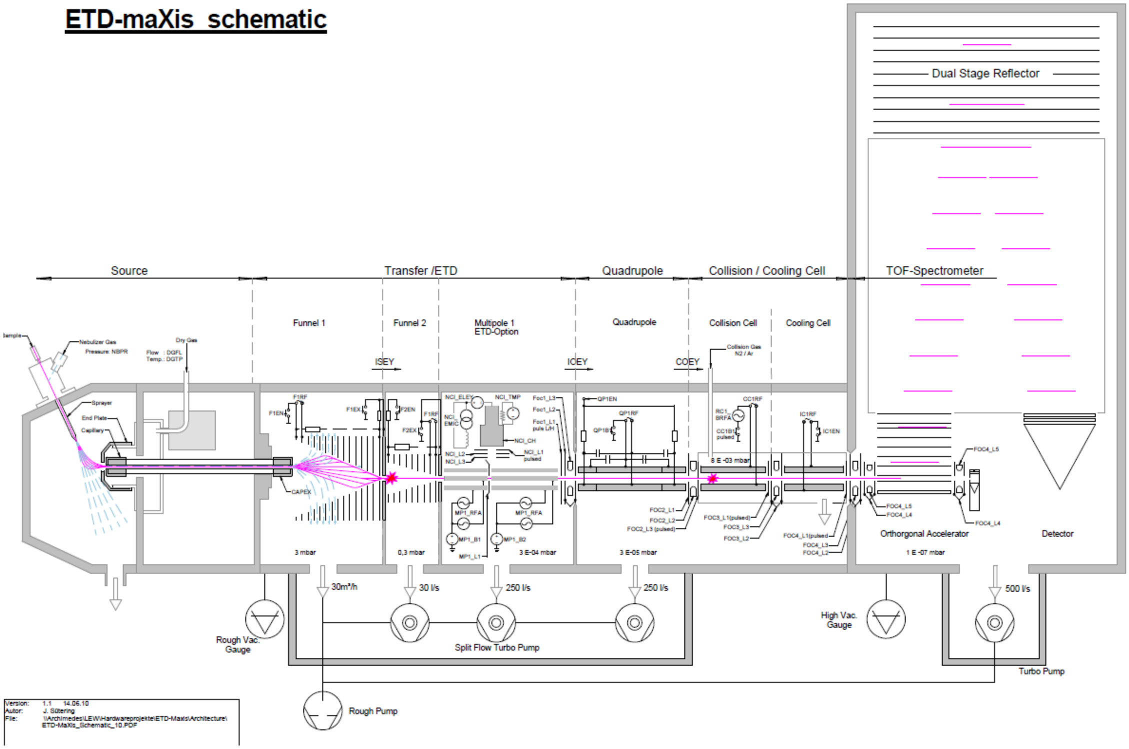


Figure A-1 maXis ETD schematic

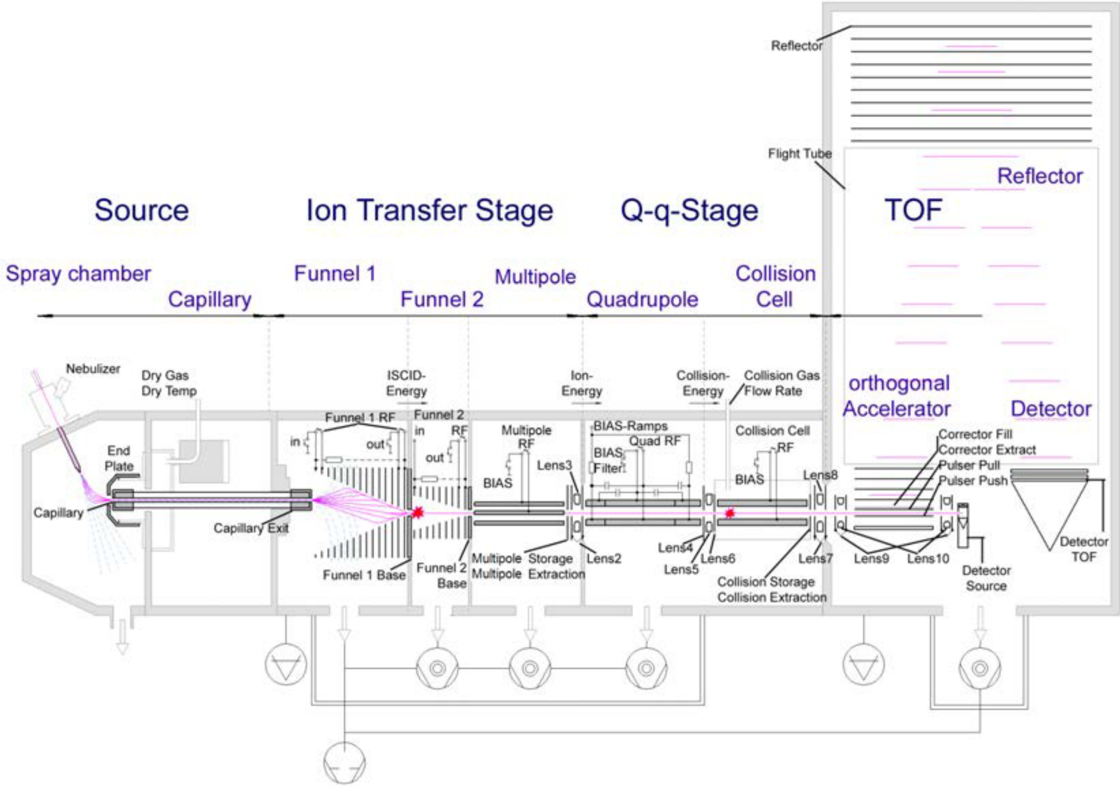


Figure A-2 maXis HD schematic

A.3 Divert Valve Connection Examples

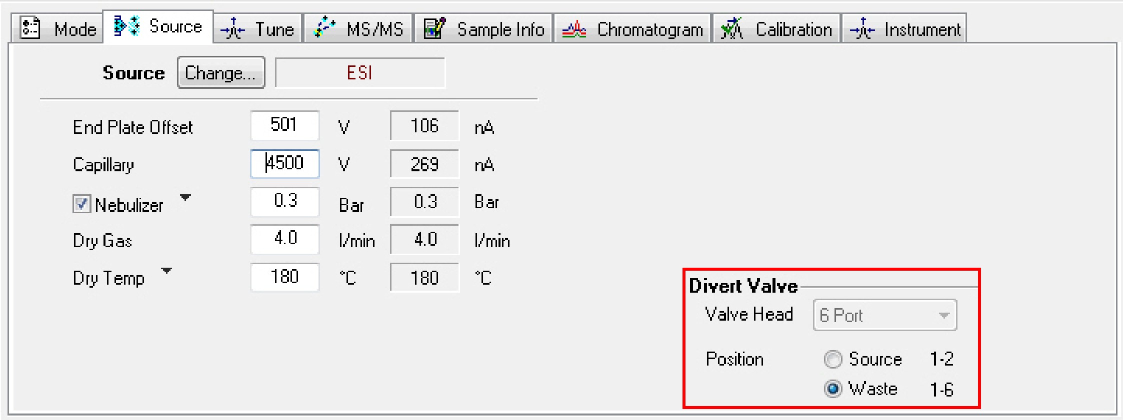


Figure A-3 Divert valve settings dialog in otofControl

otofControlallows the eluent either to be directed into the ion source or to the waste via the divert valve.

The divert valve may be used to direct the solved sample either into the source or to the waste. The selected flow path is controlled in otofControl(see Figure A-3).

A.3.1 Example 1: Sample flow through the divert valve with loop

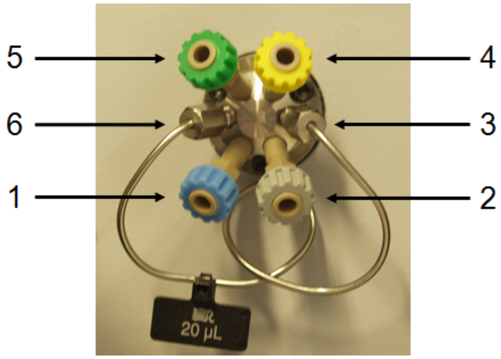


Figure A-4 Ports configured for sample flow through the divert valve with a loop

Initial configuration of the valve ports:

- Port 1: (blue) - connect to the calibrant syringe pump.
- Port 2 (gray) - connect to waste.
- Port 3 - connect by loop to port 6.
- Port 4 - (yellow) - connect to sprayer.
- Port 5 - (green) connect to the HPLC.

This configuration is may be used to introduce the calibrant at the end of the HPLC run.

Select **Source** on the **Source** page (see Figure A-3) to set the divert valve in the Source position.

- The HPLC is connected via port 5 (green) to port 4 (yellow) and the sprayer.
- The calibrant syringe is connected via port 1 (blue) to port 6 and the loop and then via port 3 to port 2 (gray) and the waste.

In the source position, the loop will be filled with calibrant.

Select **Waste** on the **Source** page to set the divert valve to the **Waste** position:

- Port 5 (green), connected to the HPLC, is directed via the loop to Port 4 (yellow) and the sprayer. The exact quantity of calibrant contained in the loop is injected to the source.
- Port 1 (blue), connected to the calibrant syringe, is then connected with Port 2 (gray) and directly to waste.

Conclusion:

- Constant flow irrespective of valve position.
- Loop must be filled during runtime of the LC analysis.
- Filling time of loop should be optimized with flow rate of syringe.
- Calibration is undertaken by post processing software (this is not a feature of otofControl).

A.3.2 Example 2: Sample flow through the divert valve without loop

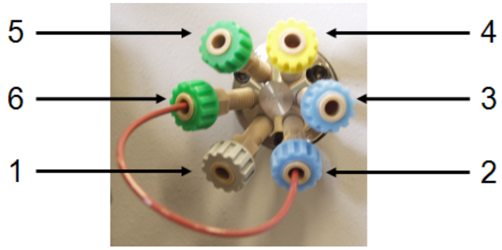


Figure A-5 Ports configured for sample flow through the divert valve without loop

Initial configuration of the valve ports:

- Port 1: (gray) - connect to the waste
- Port 2 (blue) - connect to port 6 using a capillary.
- Port 3 (blue)- connect to calibrant syringe pump.
- Port 4 - (yellow) - connect to sprayer.
- Port 5 - (green) connect to the HPLC.

Select **Waste** on the **Source** page (see Figure A-3) to set the divert valve in the Waste position.

- The HPLC is connected via port 5 (green) to port 4 (yellow) and the sprayer.
- The calibrant syringe is connected via port 3 (blue) to port 2 (blue) and via the capillary to port 6 (green) and then to port 1 (gray) and the waste.

Select **Source** on the **Source** page to set the divert valve to the **Source** position:

- Port 3 (blue), connected to the calibrant syringe pump, is directed to port 4 (yellow) and the sprayer. Calibrant will be injected to the source.
- Port 5 (green), connected to the HPLC, is now directed via Port 6 (green) and the capillary to port 2 (blue) and port 1 (gray) to waste.

Conclusion:

- Flow is not constant. The flow rate depends on the valve position (HPLC flow rate may be greater or less than the syringe flow rate).
- Calibration can be done in otofControl software or in post processing software.
- Valve can be used for switching HPLC flow directly to waste.
- Syringe pump can be used for infusions.

A.3.3 Example 3: Sample flow through the divert valve without loop

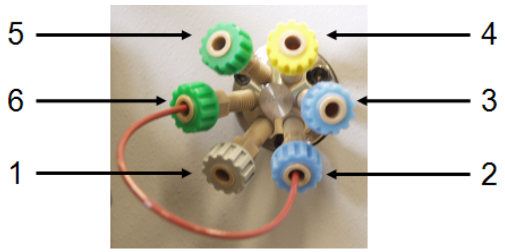


Figure A-6 Sample flow through the divert valve without loop

Divert valve in source position:

- green (HPLC) to yellow (sprayer).
- blue (calibrant) via loop to gray (waste).

Divert valve in waste position:

- green (HPLC) is connected to gray (waste) > HPLC flow is not connected to source (this is useful for flushing HPLC or column).
- blue (calibrant) is connected to yellow (sprayer).

Conclusion:

- no constant flow, flow rate is dependent on valve position (HPLC flow ⇆ syringe flow).
- calibration can be done in otofControlsoftware or in post processing software.

- valve can be used for switching HPLC flow directly to waste.
- syringe pump can be used for infusions.
- tly to waste.
- syringe pump can be used for infusions.

A.4 Values and Ranges in otofControl

Group	Description GUI	Unit	Typic.[1]	Min	Max	I/M[2]	P[3]
Source							
	End Plate Offset	V	-500	0	+6000	I	P
	Capillary	V	+4000	0	+6000	I	P
	Sprayer	bar	0,4	0	6	I	
	Dry Gas	L/min	4	0	12	I	
	Dry Temp	°C	180	0	350	I	
Transfer							
	ISCID-Energy	eV/z	0	-200	+200	M	P
	Capillary Exit	V	+170	-500	+500	I	P
	Funnel 1 in	V	+160	-500	+500	I	P
	Funnel 1 out	V	+41,5	-500	+500	I	P
	Funnel 1 RF	Vpp	300	0	+400	M	
	Funnel 1 Base	V	+41,5	-300	+300	I	P
	Funnel 2 in	V	+41,5	-300	+300	I	P

[1] *Typical values for: continuous sample introduction (3 µL/min), positive ions, no fragmentation and MS full scan.*
[2] *I = Instrument- M = Method*
[3] *These values are set according to the polarity (polarity switch for pos./neg. ions)*

Group	Description GUI	Unit	Typic.[1]	Min	Max	I/M[2]	P[3]
	Funnel 2 out	V	+41,5	-300	+300	I	P
	Funnel 2 RF	Vpp	400	0	+600	M	
Transfer (cont.)	Funnel 2 Base	V	+41,5	-300	+300	I	P
	Hexapole Bias	V	+40,5	-300	+300	I	P
	Hexapole RF	Vpp	300	0	+800	M	
	Hexapole Storage	V	+50	-300	+300	I	P
	Hexapole Extraction	V	+40	-300	+300	I	P
	Focus 1 Lens 2	V	+40	-300	+300	I	P
	Focus 1 Lens 3	V	-39	-300	+300	I	P
Quadrupole							
	Ion Energy	eV/z	+5	-200	+200	M	P
	Bias Ramps	V	+35,5	-300	+300	I	P
	Bias Filter	V	+35,5	-200	+200	I	P
	Quad RF	Vpp	autom.	0	+3800	M	
	Isolation Mass	m/z	300	0	+3000	M	
	Isolation Width	m/z	0	0	+300	M	
Collision Cell							
	Collision Energy	eV/z	10	-200	+200	M	P

[1] *Typical values for: continuous sample introduction (3 µL/min), positive ions, no fragmentation and MS full scan.*
[2] *I = Instrument- M = Method*
[3] *These values are set according to the polarity (polarity switch for pos./neg. ions)*

Group	Description GUI	Unit	Typic.[1]	Min	Max	I/M[2]	P[3]
	Focus 2 Lens 1	V	+35	-300	+300	I	P
	Focus 2 Lens 2	V	-20	-300	+300	I	P
	Focus 2 Lens 3	V	+28	-300	+300	I	P
	Collision Cell Bias	V	+25,5	-100	+100	I	P
	Collision Cell RF	Vpp	1500	0	2100	M	
	Collision Storage	V	+40	-300	+300	I	P
	Collision Extraction	V	+24	-300	+300	I	P
	Transfer Time	µs	120	0	3000	M	
	PrePulse StorageTime	µs	10	0	3000	M	
	Focus 3 Lens 2	V	+5	-300	+300	I	P
	Focus 3 Lens 3	V	-95	-300	+300	I	P
	Focus 3 Lens 4	V	0	-100	+100	I	P
	Focus 3 Lens 5	V	-20	-100	+100	I	P
	Collision Gas checkbox	on/off	1	0	+1	I	
	Flow Rate	%	+35	5	+100	I	

[1] *Typical values for: continuous sample introduction (3 µL/min), positive ions, no fragmentation and MS full scan.*
[2] *I = Instrument- M = Method*
[3] *These values are set according to the polarity (polarity switch for pos./neg. ions)*

A.5 Patents

Ref.	Key Word, Marketing	Patent DE	Patent GB	Patent US
19	glass capillary	DE 195 15 271 C2	GB 2 300 295 B	US 5,736,740 A
25	Apollo II - Ion Funnel Source	DE 195 23 859 C2	GB 2 302 985 B	US 5 572 035 A
88	gridless orthogonal accelerator		GB 2 361 353 B	US 6,717,132 B2
99	ultrastable electronics	DE 101 09 917 B4	GB 2 375 654 B	US 6,723,983 B2
107	digital threshold		GB 2 385 982 B	US 6,836,742 B2
110	focus - ion optics	DE 101 58 924 B4	GB 2 386 751 B	US 6,903,332 B2
112	adjustable reflector - detector		GB 2 387 962 B	
115	focus - signal processing enabling TIP	DE 102 06 173 B4	GB 2 390 936 B	US 6,870,156 B2
131	Apollo II - Ion Funnel Source		GB 2 402 261 B	US 7,064,321 B2
154	high precision multipole rod systems		GB 2 416 915 A	

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